HARBEN LECTURES 1899

WILLIAM R. SMITH M. D.

To

Sir Joseph Fayrer Bart
M.D., K.C.S.I. &c
with the very kind regards
of the Harben Lecturer
for 1899

Telegraphic Address:
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28. Feb.

My dear Sir Joseph

Please do me the favor of accepting the accompanying book.

Yours sincerely

William N. Smith.

Case 1.

To

Sir

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To

Sir

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DIPHTHERIA:

8.

BEING

The Harben Lectures

DELIVERED IN 1899

BEFORE

THE ROYAL INSTITUTE OF PUBLIC HEALTH,

IN THE LECTURE THEATRE OF

THE ROYAL COLLEGES OF PHYSICIANS AND SURGEONS, LONDON

BY

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President of the Royal Institute of Public Health.

LONDON:
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1900.

To

SIR HENRY HARBEN, J.P., D.L.,

THESE LECTURES ARE DEDICATED,

IN GRATEFUL RECOGNITION OF HIS MANY EFFORTS TO PROMOTE

THE PROGRESS OF PUBLIC HEALTH WORK.

DIPHTHERIA

LECTURE I.

In the course of the three lectures which it is my privilege this year to give under the terms of the Harben Trust of our Royal Institute, I shall endeavour to deal as exhaustively as I can with that most interesting disease Diphtheria—interesting to us from whichever point of view its study be approached, whether from the standpoint of its spread, its etiology, its treatment, or its prevention. And in thus dealing with the subject, I shall have occasion to draw largely upon the experience I have obtained first as Medical Officer of the School Board for London, and secondly as Chairman of the Medical Sub-Committee of the Metropolitan Asylums Board, to which Sub-Committee was entrusted the superintendence of the bacteriological examination of the diphtheria cases admitted into the hospitals of the Board over a prolonged period, and also the arrangements in connection with the preparation and supply of the antitoxic serum for the treatment of diphtheria cases.

The disease appears to have been known in the earliest ages, for the writings of Hippocrates, Galen, Celsus, and others, indicate that it was recognised by them.

In England, in 1389, there was an epidemic of sore throat which carried off a large number of children, and in the district of the Rhine, in 1517, there is recorded a prevalence of an unknown disease, in which the patients' tongues and throats were covered with a white fungoid growth. From this time the

disease seems to have visited Spain, Portugal, and Italy; in 1736 it was very prevalent in England and America, and during the years 1745-50 it not only again occurred in Portugal and Italy, but for the first time appeared in France and Holland, and again in England, especially in Cornwall and notably at Liskeard. In 1752 it was epidemic in Switzerland, Germany, and America, and later in Portugal, the North of France, Holland, Germany, America, and England. Towards the close of the eighteenth century there was, except in France, a marked remission which lasted for the first half of the present century, when the disease again appeared on a more extended scale, but during the remission sporadic cases occurred in Great Britain; in 1840 there was an epidemic in Haverfordwest, and in 1855 one at Launceston.

You will remember that it was in the year 1821 that Bretonneau, in certain memoirs submitted by him to the Académie Royale de Médecine in Paris, based upon his experience of an epidemic in Tours in 1818-21, first suggested the names "diphtheritis" and "diphtheria," as indicative of a certain specific inflammation; and he maintained that although there were at that time many differently named diseases associated with inflammation of the fauces and the upper part of the air-passages, together with the formation of a false membrane, yet that in fact these were all one and the same disease, differing it may be in certain clinical details, but agreeing anatomically; and in this connection he pronounced himself a firm adherent to the dictum of Laennec, that diseases cannot be more certainly distinguished than by their anatomical characters. This eminent physician many years after admitted the error of his then conclusions.

In illustration of the persistency of the disease in France, and the possibility of transporting the virus by human agency, it may be noted that in the Crimea the French troops suffered much from diphtheria.

According to Hirsch, a new era of prevalence of the disease began about 1857 in Europe and North America; and in England the mortality was very great in 1858-59.

From this brief outline of its history, there would appear to be no doubt that the disease has been known for many centuries,

and, further, that one decided remission occurred, which was, however, followed by a sudden outbreak over a very greatly extended area.

In England the Registrar-General has only separately abstracted diphtheria deaths since the year 1855; up to that time such deaths as occurred were classified under the head of scarlet fever.

The following table gives the death-rates per million from diphtheria in England and Wales since 1855, and in London since 1859:

TABLE I.

Showing the death-rate per million of the population from diphtheria in England and Wales since 1855, *and in London since* 1859.

YEAR.	ENGLAND AND WALES. Death-rates per Million.	LONDON. Death-rates per Million.	YEAR.	ENGLAND AND WALES. Death-rates per Million.	LONDON. Death-rates per Million.
1855	20	—	1877	111	88
1856	32	—	1878	140	155
1857	82	—	1879	120	155
1858	339	—	1880	109	144
1859	517	284	1881	121	172
1860	261	174	1882	152	222
1861	225	239	1883	158	244
1862	241	255	1884	186	241
1863	315	275	1885	164	227
1864	261	207	1886	149	212
1865	196	144	1887	160	235
1866	140	152	1888	171	319
1867	120	145	1889	189	391*
1868	137	158	1890	179	331
1869	117	107	1891	173	340
1870	120	104	1892	222	461
1871	111	105	1893	318	761
1872	93	80	1894	292	624
1873	108	95	1895	260	535
1874	150	122	1896	292	599
1875	142	167	1897	246	509
1876	129	109	1898	239	394

* The Infectious Diseases (Notification) Act came into operation in London in October, 1889.

From this it will be seen that the deaths rose gradually during the years 1855, 1856, 1857, and then with a bound in the years 1858 and 1859; but during these latter years it should be noted that scarlet fever also was prevalent, and there may have been some inaccuracies in diagnosis. In 1860 the mortality fell nearly one-half, and after a recrudescence between 1861 and 1864 it fell almost continuously until it reached a minimum in 1872. There was a slight rise in 1874 to 1876, after which the rate again became very low both for all England and for London. From 1878, however, there was a steadily increasing prevalence, slow at first, but afterwards more rapid, especially in London. In 1893 the all-England rate reached 318 per million, which is the highest since 1859, and the London rate was as high as 761 per million, or more than double the rate in London in any previous year except 1892. Since 1893 the rates have shown a tendency to decrease; this has been most marked in London, and may be partially if not wholly accounted for by improved methods of treatment.

In the following table the diphtheria death-rates in England and Wales, and in London, in various periods up to 1897, are given for each of the first five years of age, and for groups of ages afterwards:

TABLE II.

Diphtheria death-rates per million living at various age-periods.

	Period.	All ages.	0-1	1-2	2-3	3-4	4-5	5-10	10-15	15-20	20 and upwards.
England and Wales	1861-70	187	581	909	803	832	736	393	136	59	26
	1871-80	121	287	489	483	580	517	291	88	33	17
	1881-90	163	282	685	773	896	848	424	100	36	17
	1891-97	258	536	1,415	1,446	1,621	1,489	629	120	38	17
London	1861-70	179	755	1,197	1,060	912	715	296	64	35	26
	1871-80	122	318	573	628	695	660	289	55	24	17
	1881-90	259	534	1,533	1.598	1,750	1,553	601	96	32	20
	1891-97	547	1,259	3,813	3,667	3,754	3,345	1,276	182	48	25

From this the enormous increase in the mortality for ages up to five will be apparent.

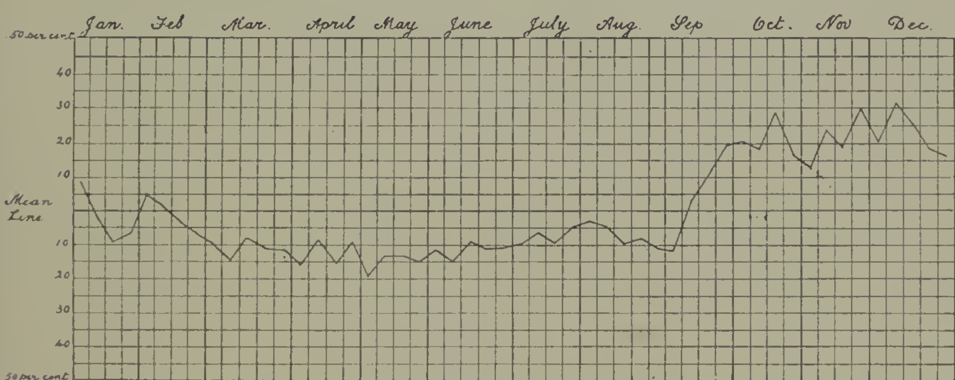
The following table gives comparatively the mortality per million of the population for several decades in England and Wales and in the Metropolis, together with that from 1891-98; the enormous increase in the London area during the periods 1881-90 and 1891-98 is most noticeable.

TABLE III.

Mortality per million of the population from diphtheria in England and Wales, and in London.

YEAR.	ENGLAND AND WALES. Death-rate per Million.	LONDON. Death-rate per Million.
1861-70 - - -	187	179
1871-80 - - -	121	122
1881-90 - - -	163	259
1891-98 - - -	255	528

Diphtheria is more prevalent in temperate and cold regions than in the tropics, and in London both the mortality and the prevalence are greatest during the quarter ending December, and lowest in the quarter ending June. Hirsch has shown that the same seasonal relationship exists in Sweden, Berlin, St. Petersburg, Vienna, and Philadelphia. The London mortality is well shown by the following curve for the thirty-eight years 1861-98.



I now propose, in the first place, to draw particular attention to the evidence which can be obtained from statistics bearing upon the mortality from diphtheria in the past, so far as such statistics affect the country at large ; I shall then deal more particularly with the statistical evidence available for London ; and thirdly with that of other large European and American cities.

In the early history of the disease there is a distinctly marked tendency for the higher mortality rate to prevail in the less densely-populated districts ; this Dr. Longstaff showed in a report

published in 1887. The report reveals also an important change in the incidence of the disease, as judged by its mortality, in the latter periods for which the observations were made.

TABLE IV.

Showing the death-rates from diphtheria according to the density of population.

Period.	Sparse.	Medium.	Dense.
1855–60	248	182	123
1861–70	223	164	163
1871–80	132	125	114

Dr. Longstaff obtained this table by grouping the registration districts of England and Wales under the headings of sparsely, medium, and densely populated, according to the relationship of the acreage to the number of the inhabitants, and it will be seen that, whereas in 1855-60 the rate in the sparsely-populated areas was more than double that in the dense districts, the rate in the decennial period 1871-80 had markedly fallen in sparsely-populated localities, whilst it was almost at the same level as in the period 1855-60 in the more crowded parts of the country.

From a communication which I have received from Dr. Longstaff in this connection, I find that some time ago he commenced to analyze the returns for the ten years 1881-90, with the result that he found considerable changes in the geographical distribution of the disease, but that so far as he went the figures did not seem to point to any very definite conclusions. He also informs me that the researches of Dr. Eigenbrodt, of Darmstadt, confirmed his principal result — viz., that diphtheria in its first incidence chiefly attacks rural districts—which he explains conjecturally as the consequence of hereditary predisposition to throat disease intensified by breeding-in.

Not only, however, has the disease during the period for which observations have been recorded varied in its incidence on locality according to the density of population, but it has also varied in its incidence in England and Wales as a whole, as will be seen by a study of the next two tables.

TABLE V.

Mean annual rates of mortality per thousand from diphtheria in English Counties, 1861-1898.

	1861-70.	1871-80.	1881-90.	1891-98.
ENGLAND AND WALES	·19	·12	·16	·26
London	·18	·12	·26	·53
Surrey	·20	·16	·23	·28
Kent	·21	·15	·23	·36
Sussex	·28	·17	·23	·29
Hampshire	·15	·11	·24	·19
Berkshire	·15	·12	·19	·18
Middlesex	·14	·15	·28	·32
Hertfordshire	·12	·10	·23	·19
Buckinghamshire	·10	·06	·16	·23
Oxfordshire	·14	·13	·09	·23
Northamptonshire	·18	·07	·12	·12
Huntingdonshire	·39	·09	·18	·15
Bedfordshire	·15	·16	·21	·21
Cambridgeshire	·30	·09	·25	·20
Essex	·22	·13	27	·46
Suffolk	·25	·10	·14	·28
Norfolk	·40	·10	·18	·23
Wiltshire	·12	·08	·13	·18
Dorsetshire	·15	·10	·16	·16
Devonshire	·13	·10	·12	·16
Cornwall	·11	·13	·16	·17
Somersetshire	·09	·09	·15	·14
Gloucestershire	·14	·09	·09	·19
Herefordshire	·13	·15	·12	·19
Shropshire	·23	·19	·17	·23
Staffordshire	·17	·11	·08	·21
Worcestershire	·16	·15	·10	·20
Warwickshire	·28	·19	·13	·23
Leicestershire	·12	·10	·10	·25
Rutlandshire	·17	·16	·07	·17
Lincolnshire	·32	·13	·16	·17
Nottinghamshire	·16	·07	·16	·10
Derbyshire	·16	·08	·09	·14
Cheshire	·23	·17	·12	·23
Lancashire	·16	·12	·15	·18
West Riding	·16	·09	·11	·16
East Riding	·23	·11	·09	·13

TABLE V. (*continued*).

Mean annual rates of mortality per thousand from diphtheria in English Counties, 1861-98.

	1861-70.	1871-80	1881-90.	1891-98.
North Riding - - -	·24	·12	·10	·15
Durham - - -	·13	·09	·08	·15
Northumberland - - -	·21	·13	·11	·16
Cumberland - - - -	·19	·10	·09	·12
Westmorland - - -	·16	·11	·09	·15
Monmouthshire - - -	·12	·15	·18	·23
South Wales - - - -	·18	·15	·10	·29
North Wales - - -	·29	·20	·17	·25

The rates for 1871-80 are taken from the Registrar-General's Decennial Supplement for 1871-80; the rates for the other periods have been calculated from the figures in his Annual and Quarterly Reports.

The figures for the period prior to 1861 have not been included in the table, as it appears somewhat doubtful whether they belong to a period of six years or to less, and therefore trustworthy average annual rates could not be obtained.

Looking at the figures for the whole country, a sharp fall in the rate occurred in the decade 1871-80 as compared with the preceding period; in 1881-90 a rise occurred, but not sufficient to bring the rate to its level in 1861-70; but in 1891-98 a further rise took place, bringing the mean rate for the eight years to a higher figure than had been reached in any previous single year since 1864. Reference to Table I. will, however, show that the mean rate in 1860-64 was slightly higher than that in the last eight years, and that the rates in the two years 1858 and 1859 had both been higher than the rate in any one of the years 1891 to 1898. For the whole country, then, the diphtheria mortality in recent years has been high, but not so high as it was a generation earlier.

Turning, however, to the separate counties, remarkable variations are at once apparent. It is true that the decrease of mortality in 1871-80 was, with a few insignificant exceptions, shared by the whole country. But not so the increase of mortality of the periods 1881-90 and 1891-98, which was very considerably greater in the southern than in the northern parts of the country. This

will be well seen if a line be drawn across the map of England, starting from Yarmouth, passing north and west of Suffolk, then south of Cambridgeshire, Hunts, Northamptonshire, Warwickshire, and Worcestershire, east and north of Herefordshire, and along the line separating South from North Wales. In every one of the twenty-two counties to the *south* of this line the diphtheria rate was higher, either in 1881-90 or in 1891-98, than it had been in 1861-70; on the other hand, only five of the twenty-three counties to the north of the line—viz., Leicester, Staffordshire, Worcestershire, Lancashire, and Durham—had higher rates, either in 1881-90 or in 1891-98, than they had had in 1861-70.

A convenient method of showing the *distribution* of diphtheria through the country independently of its special severity at any time is to represent the rates of mortality in the various counties by the proportions they bear to the rate in the whole country at the same period. Table VI. has been prepared on this plan, and by its help some important facts may be at once observed. Perhaps the most significant of these facts is that certain counties have, *in each of the four periods*, had diphtheria death-rates exceeding that for the whole country. These counties are Surrey, Kent, Sussex, and Essex. The rate for London and for one other county (Middlesex) was less than that for the whole country in 1861-70, but greater in each of the other periods; and the rates for Shropshire and North Wales were greater than the rate for the whole country in the first three periods, but less in 1891-98.

Table VI.

The mean annual rate of diphtheria mortality per thousand in each County, that for England and Wales being taken as 100.

	1861-70.	1871-80.	1881-90.	1891-98.
England and Wales -	100	100	100	100
London - - - -	96	101	160	207
Surrey - - - -	109	132	141	110
Kent - - - -	114	124	141	142
Sussex - - - -	152	141	141	113
Hampshire - - -	82	91	147	73
Berkshire - - -	82	99	117	71
Middlesex - - -	76	124	172	125

TABLE VI. (*continued*).

The mean annual rate of diphtheria mortality per thousand in each County, that for England and Wales being taken as 100.

	1861-70.	1871-80.	1881-90.	1891-98.
Hertfordshire	65	83	141	74
Buckinghamshire	54	50	98	89
Oxfordshire	76	107	55	88
Northamptonshire	98	58	74	49
Huntingdonshire	212	74	110	59
Bedfordshire	82	132	129	84
Cambridgeshire	163	74	153	78
Essex	120	107	166	182
Suffolk	136	83	86	109
Norfolk	217	83	110	89
Wiltshire	65	66	80	72
Dorsetshire	82	83	98	64
Devonshire	71	83	74	62
Cornwall	60	107	98	65
Somersetshire	49	74	92	53
Gloucestershire	76	74	55	75
Herefordshire	71	124	74	75
Shropshire	125	157	104	90
Staffordshire	92	91	49	81
Worcestershire	87	124	61	79
Warwickshire	152	157	80	89
Leicestershire	65	83	61	99
Rutlandshire	92	132	43	65
Lincolnshire	174	107	98	66
Nottinghamshire	87	58	98	41
Derbyshire	87	66	55	55
Cheshire	125	141	74	91
Lancashire	87	99	92	70
West Riding	87	74	67	63
East Riding	125	91	55	51
North Riding	130	99	61	59
Durham	71	74	49	57
Northumberland	114	107	67	61
Cumberland	103	83	55	45
Westmorland	87	91	55	58
Monmouthshire	65	124	110	91
South Wales	98	124	61	115
North Wales	158	165	104	99

GEOGRAPHICAL DISTRIBUTION OF DIPHTHERIA MORTALITY IN ENGLAND AND WALES, 1861-1870.

The average rate in England and Wales was 0·18 per 1000.

The figures printed show the rates in the several counties; and counties whose rates differed *more than 10 per cent.* from the English rate are coloured according to their departure from this rate—shades of yellow indicating *excess* of diphtheria, and shades of blue *comparative freedom* from diphtheria.

W. & A. K. Johnston Lithographers Edinburgh & London

Rates not exceeding 50 per cent. of the English rate
From 50 to 70 per cent. . . . .
" 70 to 90 " . . . .
" 90 to 110 " . . . .

From 110 to 130 per cent. of the English rate
" 130 to 150 " . . . . .
Exceeding 150 " . . . . .

GEOGRAPHICAL DISTRIBUTION OF DIPHTHERIA MORTALITY IN ENGLAND AND WALES, 1871-1880.

The average rate in England and Wales was 0·12 per 1000.

The figures printed show the rates in the several counties; and counties whose rates differed *more than 10 per cent.* from the English rate are coloured according to their departure from this rate—shades of yellow indicating *excess* of diphtheria, and shades of blue *comparative freedom* from diphtheria.

Rates not exceeding 50 per cent. of the English rate
From 50 to 70 per cent. . . . . .
,, 70 to 90 ,, ...
,, 90 to 110 ,, ...

From 110 to 130 per cent. of the English rate
,, 130 to 150 ,, ...
Exceeding 150 ,, ...

GEOGRAPHICAL DISTRIBUTION OF DIPHTHERIA MORTALITY IN ENGLAND AND WALES, 1881-1890.

The average rate in England and Wales was 0·16 per 1000.

The figures printed show the rates in the several counties; and counties whose rates differed *more than 10 per cent.* from the English rate are coloured according to their departure from this rate—shades of yellow indicating *excess* of diphtheria, and shades of blue *comparative freedom* from diphtheria.

W. & A. K. Johnston. Lithographers. Edinburgh & London.

Rates not exceeding 50 per cent. of the English rate	From 110 to 130 per cent. of the English rate
From 50 to 70 per cent.	,, 130 to 150 ,, ...
,, 70 to 90 ,, ...	Exceeding 150 ,, ...
,, 90 to 110 ,, ...	

GEOGRAPHICAL DISTRIBUTION OF DIPHTHERIA MORTALITY IN ENGLAND AND WALES, 1891-1898

The average rate in England and Wales was 0·255 per 1000.

The figures printed show the rates in the several counties; and counties whose rates differed *more than 10 per cent.* from the English rate are coloured according to their departure from this rate—shades of yellow indicating *excess* of diphtheria, and shades of blue *comparative freedom* from diphtheria.

W. & A. K. Johnston, Lithographers, Edinburgh & London.

Rates not exceeding 50 per cent. of the English rate
From 50 to 70 per cent. . . . . .
" 70 to 90 " . . . . .
" 90 to 110 " . . . . .

From 110 to 130 per cent. of the English rate
" 130 to 150 " . . . . .
Exceeding 150 " . . . . .

The results for the period 1861-98, shown in Tables V. and VI., are well combined in the accompanying maps. The actual diphtheria death-rate is shown in figures under the name of each county, and the counties whose rates differed by more than 10 per cent. from that of the whole country are coloured yellow or blue, shades of yellow indicating degrees of excessive diphtheria mortality, and shades of blue indicating relative freedom from the disease. In each case the deeper shade shows the greater departure from the average.

If, with the aid of such maps, we attempt to trace the spread of diphtheria in the south-eastern corner of England, we find that in 1861-70 London—with a rate slightly less than that of the entire country—was partly surrounded on the east and south by counties whose diphtheria mortality was relatively high. In 1871-80 the mortality in London still remained practically equal to that of England and Wales (which had fallen by one-third), but the ring of relatively diphtheritic counties had become complete around it, and in the two following periods the mortality in London itself increased enormously. Another point which is clearly brought out is that although the death-rates from diphtheria in several of the northern counties exceeded the rate in the whole country in 1861-70 and 1871-80, the excessive mortality has, during the last eight years, been confined to the south-eastern part of the country and to Monmouthshire and South Wales.

A general statement that the *southern counties* of England have suffered their highest diphtheria rates since 1881, and that the *midland* and *northern counties* (excepting Leicester, Lancashire, and Durham) had suffered theirs before 1871, is very near the truth ; and it must be noted that this southern area includes not only London and the immediately surrounding counties, but a number of agricultural counties, which cannot by any stretch of the imagination be supposed to be constantly infected from London ; and, on the other hand, the northern area of low diphtheritic rates since 1871 comprises thickly-populated towns and congeries of towns, in which all the influences of mere aggregation in the spread of the disease are likely to be as active as in

London, and *far more active* than in such agricultural districts as Bucks, Oxfordshire, and Suffolk, counties whose recent diphtheria rates exceed those shown in any of the four periods in Lancashire.

In the hope of throwing an indirect light on the problem, the mortality from measles and from scarlet fever in the English counties in the three decennia 1861-70, 1871-80, and 1881-90, and in the eight-year period 1891-98 has been calculated.

TABLE VII.

Mean annual rates of mortality per thousand from measles in English Counties, 1861-98.

	1861-70.	1871-80.	1881-90.	1891-98.
ENGLAND AND WALES	·44	·38	·44	·43
London	·57	·51	·63	·61
Surrey	·34	·26	·27	·26
Kent	·32	·23	·27	·27
Sussex	·24	·17	·23	·24
Hampshire	·30	·28	·29	·32
Berkshire	·28	·24	·28	·23
Middlesex	·33	·32	·39	·34
Hertfordshire	·28	·26	·31	·23
Buckinghamshire	·31	·27	·32	·31
Oxfordshire	·28	·20	·29	·28
Northamptonshire	·48	·33	·37	·41
Huntingdonshire	·29	·14	·17	·15
Bedfordshire	·31	·23	·27	·25
Cambridgeshire	·34	21	·22	·17
Essex	·27	·22	·37	·39
Suffolk	·23	·14	·22	·21
Norfolk	·25	·15	·20	·21
Wiltshire	·32	·21	·22	·22
Dorsetshire	·27	·20	·25	·19
Devonshire	·43	·50	·35	·33
Cornwall	·46	·23	·27	·24
Somersetshire	·30	·27	·31	·32
Gloucestershire	·38	·33	·36	·34
Herefordshire	·16	·16	·24	·13
Shropshire	·28	·19	·18	·17
Staffordshire	·58	·40	·51	·57
Worcestershire	·33	·26	·36	·31

TABLE VII. (*continued*).

Mean annual rates of mortality per thousand from measles in English Counties, 1861-98.

	1861-70.	1871-80.	1881-90.	1891-98.
Warwickshire	·52	·34	·44	·43
Leicestershire	·50	·39	·34	·42
Rutlandshire	·25	·16	·18	·13
Lincolnshire	·20	·18	·17	·16
Nottinghamshire	·36	·30	·35	·39
Derbyshire	·39	·37	·39	·42
Cheshire	·47	·38	·44	·38
Lancashire	·69	·61	·71	·59
West Riding	·49	·39	·42	·44
East Riding	·31	·27	·27	·35
North Riding	·25	·25	·26	·25
Durham	·47	·41	·47	·54
Northumberland	·37	·28	·42	·44
Cumberland	·45	·44	·44	·46
Westmorland	·21	·19	·13	·21
Monmouthshire	·48	·57	·52	·56
South Wales	·33	·39	·42	·41
North Wales	·22	·25	·22	·23

From this table it will be seen that generally speaking the mortality from measles, like that from diphtheria, declined in the decade 1871-80, and rose in 1881-90. Only four counties (Devonshire, Monmouthshire, and North and South Wales) showed *greater* mortality in 1871-80 than in the previous decade; and only seven (Devonshire, Monmouthshire, North Wales, Shropshire, Leicestershire, Lincolnshire, and Westmorland) showed less mortality in 1881-90 than in 1871-80.

In the same way, as in the case of diphtheria, with the view of showing the distribution of measles through the country, independently of its special severity at any time, Table VIII. has been prepared, in which the rate for all England is taken as 100, and those for the counties compared on this basis.

TABLE VIII.

Mean annual rates of mortality per thousand from measles in English Counties, 1861-98.

	1861-70.	1871-80.	1881-90.	1891-98.
ENGLAND AND WALES	**100**	**100**	**100**	**100**
London	130	134	143	143
Surrey	77	68	61	60
Kent	73	60	61	64
Sussex	55	45	52	56
Hampshire	68	74	66	74
Berkshire	64	63	64	55
Middlesex	75	84	89	79
Hertfordshire	64	68	70	54
Buckinghamshire	70	71	73	73
Oxfordshire	64	53	66	64
Northamptonshire	109	87	84	96
Huntingdonshire	66	37	39	36
Bedfordshire	70	60	61	57
Cambridgeshire	77	55	50	40
Essex	61	58	84	91
Suffolk	57	39	45	49
Norfolk	52	37	50	48
Wiltshire	73	55	50	50
Dorsetshire	61	53	57	45
Devonshire	98	132	80	76
Cornwall	105	60	61	55
Somersetshire	68	71	70	76
Gloucestershire	86	87	82	78
Herefordshire	36	42	55	30
Shropshire	64	50	41	39
Staffordshire	132	105	116	133
Worcestershire	75	68	82	73
Warwickshire	118	89	100	100
Leicestershire	114	103	77	99
Rutlandshire	57	42	41	31
Lincolnshire	45	47	39	36
Nottinghamshire	89	97	89	90
Derbyshire	82	79	80	98
Cheshire	107	100	100	89
Lancashire	157	160	161	138
West Riding	111	103	95	103
East Riding	70	71	61	82
North Riding	57	66	59	59

GEOGRAPHICAL DISTRIBUTION OF MEASLES MORTALITY IN ENGLAND AND WALES, 1891-1898.

The average rate in England and Wales was 0·429 per 1000.

The figures printed show the rates in the several counties; and counties whose rates differed *more than 10 per cent.* from the English rate are coloured according to their departure from this rate—shades of crimson indicating *excess* of measles, and shades of blue *comparative freedom* from measles.


SOUTH WALES 0·41
HEREFORD 0·13
WORCESTER 0·31
WARWICK 0·43
NORTHAMPTON 0·41
BRIDGE 0·17
SUFFOLK 0·21
BEDFORD 0·25
MONMOUTH 0·56
GLOUCESTER 0·34
0·28 OXFORD
BUCKS 0·31
HERTFORD 0·23
ESSEX 0·39
MIDDLESEX 0·34
LONDON
LONDON 0·61
BERKS 0·23
WILTS 0·22
SURREY 0·26
KENT 0·27
SOMERSET 0·32
HANTS 0·32
SUSSEX 0·24
DEVON 0·33
DORSET 0·19
0·24 CORNWALL
52
51
50
5 Longitude West 4 of Greenwich 3
1
0
1
W. & A. K. Johnston. Lithographers Edinburgh & London
Rates not exceeding 50 per cent. of the English rate
From 50 to 70 per cent.
,, 70 to 90 ,,
,, 90 to 110 ,,
From 110 to 130 per cent. of the English rate
,, 130 to 150 ,,
Exceeding 150

TABLE VIII. (*continued*).

Mean annual rates of mortality per thousand from measles in English Counties, 1861-98.

	1861-70.	1871-80.	1881-90.	1891-98.
Durham - - - -	107	108	107	125
Northumberland - -	84	74	95	103
Cumberland - - -	102	116	100	107
Westmorland - - -	47	50	30	48
Monmouthshire - -	109	150	116	130
South Wales - - -	75	103	95	96
North Wales - - -	50	66	50	54

When, however, we inquire more closely into the matter, we find a remarkable difference of behaviour between diphtheria and measles. The mortality in certain counties was greater than in the country as a whole during each of the four periods. These counties were, London, Monmouthshire, Staffordshire, Lancashire and Durham. The relative freedom of the southern counties from measles is as remarkable as the liability of several of them to diphtheria. The measles rate in Northamptonshire and in Cornwall exceeded the rate in England and Wales during 1861-70, and the rate in Devonshire was excessive in 1871-80, but these are the only cases in which the rate in any southern county except London has exceeded the rate for the whole country in *any one* of the four periods. A comparison of the accompanying map with that for diphtheria will show clearly the contrast between the local distributions of measles and of diphtheria during the period 1891-98.*

Applying the same line of reasoning to cases of scarlet fever, we have in the first place the death-rates per 1,000 living for the years 1861-98.

* Corresponding maps for the years 1861-90 in reference to measles were published in THE JOURNAL OF STATE MEDICINE for May, 1896.

TABLE IX.

Mean annual rates of mortality per thousand from scarlet fever, in English Counties, 1861-98.

	1861-70.	1871-80.	1881-90.	1891-98.
ENGLAND AND WALES	·97	·72	·33	·17
London	1·14	·60	·33	·19
Surrey	·78	·27	·12	·06
Kent	·74	·34	·14	·08
Sussex	·57	·23	·12	·04
Hampshire	·71	·37	·10	·08
Berkshire	·67	·32	·15	·07
Middlesex	·79	·33	·18	·23
Hertfordshire	·76	·31	·16	·07
Buckinghamshire	·71	·35	·18	·06
Oxfordshire	·56	·38	·19	·06
Northamptonshire	·91	·40	·26	·14
Huntingdonshire	·55	·44	·14	·06
Bedfordshire	·69	·48	·27	·09
Cambridgeshire	·58	·25	·21	·04
Essex	·74	·42	·22	·13
Suffolk	·66	·46	·16	·07
Norfolk	·60	·33	·10	·09
Wiltshire	·60	·47	·12	·08
Dorsetshire	·68	·33	·11	·08
Devonshire	·59	·34	·19	·11
Cornwall	·84	·59	·17	·15
Somersetshire	·67	·47	·18	·13
Gloucestershire	·88	·49	·29	·10
Herefordshire	·58	·35	·20	·13
Shropshire	·55	·52	·20	·11
Staffordshire	1·06	1·01	·36	·23
Worcestershire	·94	·71	·25	·10
Warwickshire	1·01	·86	·29	·16
Leicestershire	·57	·62	·38	·20
Rutlandshire	·87	·49	·17	·04
Lincolnshire	·70	·51	·31	·10
Nottinghamshire	·80	·64	·43	·18
Derbyshire	·81	·79	·36	·17
Cheshire	·99	·87	·29	·18
Lancashire	1·36	1·13	·48	·25
West Riding	1·11	1·03	·53	·20
East Riding	1·08	·51	·51	·14
North Riding	·91	·67	·34	·12

Table IX. (*continued*).

Mean annual rates of mortality per thousand from scarlet fever in English Counties, 1861-98.

	1861-70.	1871-80.	1881-90.	1891-98.
Durham - - -	1·62	1·38	·51	·18
Northumberland -	1·38	1·15	·35	·16
Cumberland - - -	·89	·82	·23	·21
Westmorland - - -	·51	·42	·11	·09
Monmouthshire - -	1·04	·69	·51	·27
South Wales - - -	·98	·86	·55	·23
North Wales - - -	·76	·70	·26	·17

And here it is to be noted that the changes in scarlet fever mortality have been altogether of another kind. Table IX. shows that the tendency throughout the country has been towards a rapid and continuous decline. In the country as a whole, the mortality in 1891-98 was only a little more than one-sixth of what it had been in 1861-70, and every single county shows a much lower rate in 1891-98 than in 1861-70. Indeed, only three counties fail to show a *successive* decline of mortality in the four periods covered by the table. Of these exceptions, the increase in the scarlet fever mortality of Middlesex in 1891-98 is probably accounted for by the establishment of the Metropolitan Asylum Board's Northern and North-Eastern Hospitals in Tottenham, while the others are too small to be of real importance. Table X. has been prepared to show, as before described, the relative geographical distribution of scarlet fever in England and Wales.

Table X.

The mean annual rate of scarlet fever mortality per thousand in each County, that for England and Wales being taken as 100.

	1861-70.	1871-80.	1881-90.	1891-98.
England and Wales - -	100	100	100	100
London - - - -	118	83	100	115
Surrey - - - -	80	38	36	34
Kent - - - -	76	47	42	48
Sussex - - - -	59	32	36	25
Hampshire - - -	73	51	30	44

TABLE X. (*continued*).

The mean annual rate of scarlet fever mortality per thousand in each County, that for England and Wales being taken as 100.

	1861-70.	1871-80.	1881-90.	1891-98.
Berkshire - - -	69	44	45	39
Middlesex - - -	81	46	55	136
Hertfordshire - - -	78	43	48	39
Buckinghamshire - -	73	49	55	34
Oxfordshire - - -	58	53	58	37
Northamptonshire - -	94	56	79	85
Huntingdonshire - -	57	61	42	37
Bedfordshire - - -	71	67	82	56
Cambridgeshire - -	60	35	64	26
Essex - - - -	76	58	67	75
Suffolk - - - -	62	46	30	41
Norfolk - - - -	68	64	48	54
Wiltshire - - -	62	65	36	49
Dorsetshire - - -	70	46	33	47
Devonshire - - -	61	47	58	64
Cornwall - - -	87	82	52	89
Somersetshire - - -	69	65	55	75
Gloucestershire- - -	91	68	88	62
Herefordshire - - -	60	49	61	78
Shropshire - - -	57	72	61	66
Staffordshire - - -	109	140	109	133
Worcestershire - -	97	99	76	59
Warwickshire - - -	104	120	88	93
Leicestershire - - -	59	86	115	118
Rutlandshire - - -	90	68	52	24
Lincolnshire - - -	72	71	64	57
Nottinghamshire - -	82	89	130	108
Derbyshire - - -	84	110	109	99
Cheshire - - -	102	121	88	105
Lancashire - - -	140	157	145	150
West Riding - - -	114	114	161	120
East Riding - - -	111	71	155	82
North Riding - - -	94	93	103	68
Durham - - -	167	192	155	109
Northumberland - -	142	160	106	96
Cumberland - - -	92	114	70	127
Westmorland - - -	53	58	33	53
Monmouthshire - -	107	96	155	161
South Wales - - -	101	120	167	138
North Wales - - -	78	97	79	98

GEOGRAPHICAL DISTRIBUTION OF SCARLET FEVER MORTALITY IN ENGLAND AND WALES, 1891-1898.

The average rate in England and Wales was 0·169 per 1000.

The figures printed show the rates in the several counties; and counties whose rates differed *more than 10 per cent.* from the English rate are coloured according to their departure from this rate—shades of scarlet indicating *excess* of scarlet fever, and shades of blue *comparative freedom* from scarlet fever.

Rates not exceeding 50 per cent. of the English rate
From 50 to 70 per cent. . . . . .
" 70 to 90 " . . . . .
" 90 to 110 " . . . . .

From 110 to 130 per cent. of the English rate
" 130 to 150 " . . . . .
Exceeding 150 " . . . . .

From this table it is seen that the mortality in Staffordshire, Lancashire, the West Riding, Durham, and South Wales was in excess in each period, and in Cheshire, Northumberland, and Monmouthshire in three periods out of the four. It will be noted that Staffordshire, Lancashire, Durham, and Monmouthshire occupy a similar unhappy pre-eminence in regard to measles also; while, on the other hand, Staffordshire, Lancashire, the West Riding, and Durham are among the counties whose diphtheria rates have in each period been below those of the whole country. The similarity of the local distributions of measles and scarlet fever, and their contrast with the local distribution of diphtheria, will be still more clearly seen by an examination of the accompanying map* and by comparing it with the maps relating to diphtheria and measles.

The general result of such an examination appears to be that, although the spread of every infectious disease must necessarily be favoured by bringing together large numbers of those most liable to it, yet the conditions most favourable to the diffusion of measles and scarlet fever are not those most favourable to the diffusion of diphtheria. In other words, if we wish to explain why Sussex is comparatively free from measles (one of the most infectious, if not the most infectious disease amongst children) and scarlet fever, but suffers from excessive diphtheria mortality, while Staffordshire is comparatively free from diphtheria but suffers excessively from measles and scarlet fever, we must look for some conditions which are not common to the two counties.

It may be suggested that such a condition is found in the fact that Sussex is much nearer to London than is Staffordshire; but this suggestion fails entirely to meet the case, since the special liability of Sussex to diphtheria began several years before that of London; and, moreover, Staffordshire shares the liability of London to excessive measles mortality, while Sussex does not. Again, if, for example, school infection is the chief cause of the mortality from diphtheria in Sussex, why should Staffordshire escape? And if school infection is the chief factor in the spread of measles and scarlet fever in Staffordshire, why should Sussex

* Corresponding maps for the years 1861-90 in reference to scarlet fever were published in THE JOURNAL OF STATE MEDICINE for May, 1896.

escape? It is evident that several agencics must be at work in spreading zymotic diseases among children, and it may be taken as highly probable that the vicinity of infected centres is one, and school infection is another of those agencies. But the comparison of the geographical distributions of three of these diseases strongly suggests that special local causes other than school attendance, or the neighbourhood of infected centres, have a potent influence in selecting the disease and promoting its diffusion.

Comparison of the statistics of diphtheria mortality, Table XI., for the principal towns of America and Europe, as furnished by Dr. Arthur Newsholme, in his book on epidemic diphtheria, demonstrates two facts very clearly: firstly, that London compares very favourably with the majority of these towns in regard to its diphtheria death-rate; and, secondly, that all towns, whether endemic centres of this disease or not, are liable at varying intervals to epidemic outbursts of a severe character, lasting over a period of several years.

The value of the statistics thus brought forward is somewhat diminished from the fact that the only evidence attainable of the prevalence of the disease from year to year is from the number of deaths per 100,000 of the population, although the case mortality must have been subject to considerable variations, and is therefore not a true measure of incidence. As the author points out, however, notification has been in force for too short a period to afford reliable evidence of the prevalence of the disease over any considerable period of time.

Again, it has been necessary in some cases to group together the mortality from diphtheria and croup, that from diphtheria alone not being forthcoming. In many cases, however, the death-rates from diphtheria alone are also available.

From this table it will be seen that:

New York	has	a mean	death-rate for	27	years of	109	per 100,000
Berlin	,,	,,	,,	27	,,	101	,,
Boston	,,	,,	,,	34	,,	100	,,
Christiania	,,	,,	,,	33	,,	80	,,
Chicago	,,	,,	,,	35	,,	77	,,

—whilst the greatest mortality for any year in London was 76,

Place.	Years of Observation.	Diphtheria plus Croup.		Diphtheria alone.		Mean Death-rate.	
		Highest.	Lowest.	Highest.	Lowest.	Diphtheria plus Croup.	Diphtheria alone.
London	1859-98	—	—	76 in 1893	8 in 1872	—	26
NORTH AND SOUTH AMERICA—							
Boston	1861-95	218 in 1881	35 in 1872	163 in 1881	51 in 1891	116	100
New York	1868-95	276 in 1877	68 in 1868	208 in 1877	23 in 1873	161	109
Massachusetts	—	134 in 1880	53 in 1891	—	—	—	—
Chicago	1859-94	255 in 1860	42 in 1874	141 in 1860	20 in 1874	140	77
Buenos Ayres	1885-95	388 in 1888	61 in 1895	—	—	136	—
FRANCE—							
Paris	1865-96	121 in 1877	17·5 in 1895-6	—	—	63	—
Marseilles	1886-96	198 in 1891	28 in 1895	—	—	113	—
ITALY—							
Milan	1875-96	267 in 1874	47 in 1887	—	—	99	—
Florence	1866-90	422 in 1871	23 in 1884	—	—	83	—
Rome	1877-95	122 in 1879	8 in 1895	—	—	21	—
HOLLAND AND BELGIUM—							
Amsterdam	1879-95	—	—	72 in 1883	3 in 1879	—	31
Brussels	1862-96	113 in 1865	15 in 1881	—	—	47	—
Antwerp	1860-96	217 in 1865	17 in 1896	—	—	67	—
GERMANY—							
Hamburg	1872-95	123 in 1887	17 in 1896	—	—	49	—
Berlin	1869-96	242 in 1883	34 in 1896	220 in 1883	31 in 1896	119	101
Dresden	1878-95	253 in 1882	52 in 1895	—	—	129	—
Frankfort-on-Maine	1851-95	160 in 1890	9 in 1860	157 in 1890	7 in 1862	64	53
Munich	1868-74, 1876-95	284 in 1869	53 in 1895	—	—	99	—
AUSTRIA-HUNGARY—							
Trieste	1865-96	251 in 1873	27 in 1877	—	—	130	—
Buda-Pesth	1874-96	194 in 1878	46 in 1893	140 in 1891	29 in 1884	108	68
Vienna	1865-95	177 in 1878	42 in 1873	144 in 1888	19 in 1884	77	—
RUSSIA—							
St. Petersburg	1879-90, 1892-95	—	—	154 in 1882	27 in 1893	—	65
Moscow	1878-96	111 in 1894	35 in 1878	105 in 1893	27 in 1880	72	64
SCANDINAVIA—							
Christiania	1860-93	329 in 1887	17 in 1871	303 in 1887	1 in 1873	109	80
Gothenburg	1861-95	250 in 1873	5 in 1891	137 in 1884	3 in 1891	58	23
Stockholm	1861-96	139 in 1893	12 in 1896	121 in 1893	6 in 1878	72	45

this occurring in 1893. With regard to the maximum annual diphtheria mortality in these towns, the figures are still more striking:

In 1887	the death-rate	of	Christiania	was	303	per 100,000
In 1883	,,	,,	Berlin	,,	220	,,
In 1877	,,	,,	New York	,,	208	,,

—while Boston and Chicago in America, Frankfort-on-Maine in Germany, Buda-Pesth and Vienna in Austria-Hungary, St. Petersburg and Moscow in Russia, Gothenburg and Stockholm in Scandinavia, all furnish death-rates of considerably over 100 per 100,000; the highest corresponding figure for London, as previously stated, being 76.

When the combined death-rates from diphtheria and croup are examined, similar results are obtained, and the list of excessive mortalities is swelled by the returns from Buenos Ayres, Paris and Marseilles, Milan, Florence and Rome, Brussels and Antwerp, Dresden and Munich, and Trieste, in addition to those towns already mentioned.

In the case of Florence, the maximum mortality from these two diseases reached 422 per 100,000 in the year 1871, while the death-rates in New York, Chicago and Buenos Ayres, Milan, Dresden, Trieste, Christiania, and Gothenburg were above 250.

With regard to the maximum epidemic years of the different towns, Dr. Newsholme's figures show that not only were epidemics prevalent during different years in the different countries, but that they occurred in different years in the various towns of the same countries; and in the case of Brussels there was a difference in this respect even between the city and its suburbs, for in the course of an epidemic which reached its height in 1862, the decline was some years later in the suburbs than in the city itself, and, in fact, was scarcely over when a second epidemic overran the whole district, culminating in the year 1885.

Taking these figures into consideration, it is evident that, so far from there being at the present moment a formidable death-rate from diphtheria in London, this city has been spared in a remarkable manner from the lot which has fallen to most American and European cities of importance. Moreover, it

seems possible that the present increase in the diphtheria death-rate may be accounted for by the occurrence of a period of epidemicity of the disease, mild at present as compared with that which has been experienced by the towns of other countries in previous years, this epidemicity being due to general causes, of which we have at present no knowledge, and which we therefore cannot hope to control until that knowledge is obtained.

Now, what is the nature of this disease we call diphtheria? We recognise it to be a disease of a specific infectious character, primarily affecting mucous membranes, and most commonly the upper portions of the respiratory and digestive tracts. At first it is a purely local inflammation characterized by the formation of a false membranous deposit, the system only secondarily becoming affected.

The disease is occasioned, as we now all know, by the reception at a particular point of the affected surface of the Klebs-Löffler *Bacillus diphtheriæ*, which micro-organism must be considered as the specific and essential cause of the local complaint, whilst the general system is subsequently implicated by the absorption of the chemical poison or toxin, which is formed during the growth of the organism in the throat.

The Klebs-Löffler bacillus is so called after its discoverers. Klebs in 1883 described a special bacillus which he found in diphtheritic membranes, and Löffler not only succeeded in cultivating this organism upon different artificial media, but by a series of inoculation experiments produced in animals lesions identical with those associated with diphtheria in man.

The observations of these gentlemen were subsequently confirmed by other bacteriologists, notably by Roux and Yersin in France, and Professor Sidney Martin in this country.

This organism is always found in connection with the false membranes associated with diphtheria, and for this reason, therefore, it becomes a question of prime importance that bacteriological tests should be applied in all cases of suspected diphtheria.

The bacillus is extremely polymorphic, but two varieties may be noted—the long and the short. The long variety consists of organisms usually clubbed at one or the other end, being distinctly curved, and usually presenting when stained a granular

or segmented appearance, owing to the fact that they do not uniformly take up the dye; these clubbed forms are regarded by many as mere degeneration or involution forms, but this view is probably erroneous, as they usually are best marked in young growths.

The short forms occur usually as straight or slightly curved rods not uniform in thickness, being either slightly swollen at one end, or else possessing pointed ends, and somewhat bulbous centres.

These bacilli are generally arranged in irregularly - shaped clusters; they never form chains or threads, possess no spores, and are easily stained by Gram's method, or with any ordinary aniline dye.

Usually no difficulty occurs in recognising the diphtheria bacilli either upon the surface of the nutrient media or under the microscope, but occasionally a difficulty arises, for organisms closely resembling Klebs-Löffler bacilli are found in healthy and non-diphtheritic sore throats, which have been described as pseudo-diphtheria bacilli. Some observers give this name to organisms bearing a superficial resemblance to the true diphtheria organism, whilst others apply the term to organisms which morphologically cannot be distinguished from the typical bacillus, but which differ from it in so far as they fail to produce any pathogenic properties when injected into guinea-pigs. The exact connection of these organisms with the true bacillus is not clearly understood. Roux and Yersin have found on the same media the virulent and non-virulent varieties, and it is known that the true organism can be deprived of its virulence; indeed, many French observers hold that the pseudo-diphtheria bacilli are nothing more than the non-virulent variety of the true diphtheria bacillus. The difficulties of the subject, therefore, in this connection are obvious, and the doubts arising in the minds of non-medical persons as to the value of a bacteriological test for the disease are accounted for.

If a tube of Löffler's blood-serum be inoculated by a swab from a suspected throat and placed in an incubator, the diphtheria bacillus will, if present, manifest itself within twelve hours, owing to the fact that it gets the start of other organisms

found in the throat; but after twenty-four hours these latter will also be present, and as they grow with great rapidity, they soon obscure the colonies of the diphtheria bacillus.

The evidence justifying the assertion that the Klebs-Löffler bacillus is alone the cause of diphtheria is of a very interesting nature. True diphtheria apparently never arises spontaneously in the lower animals, with the single exception of the cat. In this animal, Dr. Klein, to whom we are much indebted for many able researches on the subject, has described a disease characterized by broncho-pneumonia, cardiac disease and ophthalmia, whilst in the consolidated portions of the lung he has found the diphtheria organism in considerable numbers. He consequently concludes that cats are susceptible to human diphtheria, and that in them the disease principally affects the lungs.

He has also shown that inoculation of the conjunctiva or of the mucous membrane of the mouth of the cat with diphtheritic material is followed by changes closely resembling the disease in the human subject.

Injection of virulent diphtheria bacilli into guinea-pigs kills them in eighteen to twenty-two hours, a swelling occurring at the seat of inoculation, caused by infiltration and exudation, this being shortly followed by degenerative changes in the heart and muscles.

Diphtheria bacilli can be recovered from the seat of inoculation and from the blood of such animals.

The loss of muscular power which accompanies or follows diphtheria in the human subject can also be produced in animals by artificial infection. The poisonous products, or toxins, resulting from the growth of the organism in broth, if inoculated into animals, cause paresis, degeneration of the nerves, and fatty degeneration of the cardiac and other muscles.

Our bacteriological knowledge of the disease has been greatly advanced by the enlightened policy of the Metropolitan Asylums Board, of whose work in connection with the treatment of infectious disease in London it is impossible to speak too highly. Consequent upon representations made to the Board, in which this Institute played no insignificant part, it was determined that

not only should bacteriological tests be instituted in all cases of suspected diphtheria, but that so far as possible these tests should —at least, in the first instance—be made upon a uniform basis, the responsibility being centred in one person; consequently, on January 1, 1895, an arrangement came into force by which the Laboratories Committee of the Royal Colleges of Physicians and Surgeons agreed to undertake on behalf of the Metropolitan Asylums Board, not only the examination of doubtful cases of diphtheria admitted to the hospitals of the Board, but also a similar examination before the cases were discharged. The work was carried out under the able superintendence of my friend Professor G. Sims Woodhead, the then director of the laboratories, and extended over a period of two years, during which time no less than 12,173 examinations were made. I am, through the kindness of the Board, permitted to refer to the report of this work which will shortly be published, and to quote the conclusions arrived at.

For the first two or three months a microscopical examination was made of the fresh secretion from the throats of the patients as soon as the material arrived at the laboratory, and in 25 per cent. of the positive cases the presence of the diphtheria bacillus could be made out; but it was just in these cases that the physician in charge had no doubt as to the nature of the disease. This preliminary examination was very soon abandoned, the cultivation method being alone relied upon.

In order that the original culture should be made with as little trouble as possible, a modification of the well-known New York outfit was adopted. It consisted of a box containing: (1) a "swab"; (2) a tube of Löffler's serum; (3) a copy of "Directions"; (4) a form on which the details of the case could be entered. A small pledget of cotton-wool attached to an iron wire with a roughened end was placed in a clean test-tube, and afterwards plugged with cotton-wool. The whole was then heated at a temperature of 160° to 170° C. for two or three hours, in order that the cotton wadding might be completely sterilized. These "swabs" were then ready for use at any moment.

During the course of these examinations a medium was pre-

pared in which decalcified blood-plasma was substituted for blood-serum, and for some considerable time during the latter part of the inquiry this medium was used. Each morning the cultures were examined microscopically. For this purpose cover-glass films were used, the staining adopted being a modification of Gram's method devised by Nicolle, consisting in the substitution of carbolic acid for aniline water, in the use of a stronger iodine solution and in the addition of acetone to the decolourizing of fluid. The staining fluid consists of 10 c.c. of a saturated alcoholic solution of gentian violet added to 100 c.c. of a 1 per cent. solution of carbolic acid. This has the great advantage over aniline water that it may be kept indefinitely. The iodine solution consists of 1 gramme of iodine, 2 grammes of iodide of potassium, and 200 c.c. of distilled water.

The fixed cover-glass preparation remains in the stain for about five seconds, and is then passed directly into the iodine fluid, where it remains for about five seconds, after which it is decolourized by being passed rapidly through a mixture of one volume of acetone with four volumes of absolute alcohol. This removes all unfixed stain almost instantly. The specimen is then at once dehydrated in xylol, allowed to dry, and mounted in balsam.

As an alternative Löffler's methylene blue solution was sometimes used: Saturated alcoholic solution of methylene blue, 30 c.c.; 0·01 per cent. solution of caustic potash, 100 c.c.

After incubation for eighteen or twenty-four hours the diphtheria colonies are rounded, elevated, and of a translucent grayish-white colour. The younger colonies are of a yellowish tinge, they have a moist surface, a slightly scalloped margin, and by transmitted light show an opaque centre due to the more active growth. At this point, if the colonies are numerous and close together, they are generally small and discrete. In older growths the colonies become flattened, the central opacity and the crenation of the edges more marked, and they lose their moist shiny appearance, becoming dull. Growth takes place at any temperature between 22° and 40°, but the best growth occurs between 35° and 37°.

The organism grows on all the ordinary alkaline media—agar,

glycerine agar, gelatine, milk, and potato (when its surface is made alkaline).

Agar forms a good medium, but the growth is not so abundant as on serum. After long cultivation on agar, the typical active diphtheria bacillus will die out; the pseudo-diphtheria bacillus grows well on this medium, as does also the less active shorter form, the growth having much the same form as the diphtheria bacillus on Löffler's serum.

The main points of difference between the colonies of the Löffler bacillus and those of the pseudo-diphtheria bacillus are, that the colonies of the latter are usually pure milk-white, flatter, more moist on the surface, softer in consistence, and exhibiting a great tendency to become confluent. The cultural differences are at best, however, but relative, and must be confirmed by growth on other media, by the reaction to litmus, by microscopic examination, and by animal experiments.

In broth the pseudo-bacillus causes a greater turbidity than Löffler's bacillus, the broth tending to become more alkaline in time. On agar and gelatine it grows more abundantly. This latter character is considered by Escherich and others to be of great diagnostic value. It grows on gelatine at a lower temperature than the true form, and will even grow at 18° C.

Another closely allied but non-pathogenic form is described as the xerosis bacillus. Probably several slightly different forms have been described under this head by different investigators, and Löffler considers that probably they all, with the diphtheria bacillus, belong to one group or natural family, and that although "all are distinguished by peculiar club formation, and by isolated stainable granules, they offer, on closer comparison, small but constant morphological and cultural differences."

The xerosis bacillus grows best on blood-serum. In broth there is a rapid flocculent growth with no formation of acid, and agar needs the addition of glycerine to produce a growth.

Another organism of frequent occurrence in cultures made from the throat is the potato bacillus, which grows most rapidly, first as a moist viscid layer, then as a corrugated membrane. It is

a troublesome adjunct, as it impedes the growth of the true organism.

Colonies of streptococci appear at the end of twenty-four hours as minute transparent, dew-like points, whilst colonies of staphylococci show a flattened, spreading, irregular, opaque, moist growth of even thickness throughout.

Escherich roughly classifies the diphtheria bacilli under three heads :

1. Short, wedge-shaped, compact forms, with rounded angles, showing no signs of differentiation into light and dark bands when stained with alkaline methylene blue. These bacilli are 1·2 to 2·0 μ long, and 0·3 to 0·5 μ broad.

2. Slender cylindrical, slightly-curved rods. These, when stained with alkaline methylene blue, and even by Gram's method, show the characteristic striping of alternate light and dark bands. They have a length of 3·5 to 4·5 μ, and a breadth of 0·4 to 0·5 μ. Professor Sims Woodhead calls this latter form long, in contradistinction to the former variety, which he designates as short.

3. Escherich's third group includes the club-shaped bacilli ; they may develop from the long group by an increase in length to as much as 6 or 8 μ, and by one or both of their ends becoming swollen.

Besides these three main groups, there are found in old cultures a number of most extraordinary forms—long spiral, sausage-like chains or strings, all of which are probably involution forms.

In virulent cases the wedge-shaped form of the first group has often been observed, sometimes two wedges placed together base to base, whilst the short ovoid forms are few in number. In milder cases the ovoid forms are more numerous, and in convalescent cases they may be the only form present.

These ovoid forms, especially those in which the staining extends throughout the bacillus, were found to be associated with a low death-rate. These organisms are usually arranged in battalion form, and are often met with in pure cultures; they correspond to the pseudo-diphtheria bacillus, and must be sharply differ-

entiated from the virulent, short, striped, ovoid, wedge-shaped bacillus of the first group.

It appears to be one of the features of the diphtheria bacillus that it never forms even moderately long chains. It often gives rise to a peculiarly characteristic angled or interlacing arrangement, the bacilli being arranged in groups of two, three, and four, either lying parallel to each other, or at a more or less open angle, or even across one another.

Escherich says that the paucity of interlocking or interlacing points to the presence of the pseudo-diphtheritic bacillus.

TABLE XII.

Table giving the number of cases admitted to the various hospitals during the several years, and also the total number of cases from which specimens were taken and cultures made, with the results of such examinations.

Hospital.	Year 1894.	Year 1895.	Year 1896.	Total cases.	Number of examinations of cases in which diphtheria bacilli were found.	Number of examinations of cases in which no diphtheria bacilli were found.	Total examinations.	Percentage of cases in which diphtheria bacilli were found.
Fountain - -	11	930	1,301	2,242	1,642	600	2,242	73·23
Western - -	—	838	1,171	2,009	1,485	524	2,009	73·91
Eastern - -	5	1,030	1,049	2,084	1,438	646	2,084	69·001
South-Eastern -	29	734	974	1,737	1,243	494	1,737	71·56
South-Western -	—	559	615	1,174	925	249	1,174	78·79
North-Western -	—	795	916	1,711	1,352	359	1,711	79·01
North-Eastern -	—	157	108	265	105	160	265	39·62
Brook - -	—	—	278	278	224	54	278	80·58
Northern - -	—	253	319	572	442	130	572	77·27
Gore Farm -	—	—	101	101	81	20	101	80·19
Total - -	45	5,296	6,832	12,173	8,937	3,236	12,173	73·41

In the Gore Farm and Northern Hospitals only fresh cases are given.

In the North-Western, South-Western, Brook, and the two Convalescent Hospitals the percentage of notified or diagnosed

cases in which diphtheria bacilli were found in the throat is very high. These figures were regular, and in each year approximated to the mean. This noteworthy point is difficult to account for, but may be of value in connection with the distribution of diphtheria in certain districts of the Metropolis, if the cases occurring in those areas were invariably admitted to these hospitals.

Table XIII.

Showing the cases at the different hospitals for 1894, 1895, *and* 1896, *in which more than one examination was made.*

Hospital.	Cases in which diphtheria bacilli were found in the last examination made.	Cases in which no diphtheria bacilli were found in the last examination made.	Cases in which the first examination was not satisfactory.	Cases with percentage in which no diphtheria bacilli were found at the first examination, but were afterwards found.		Cases in which a negative diagnosis was sent to the hospital preceded and succeeded by a positive diagnosis.	Cases in which a positive diagnosis was sent to the hospital, preceded and succeeded by a negative diagnosis.	Total cases examined on more than one occasion.
Fountain	688	954	20	178	11·3	34	7	1,205
Western	424	1,061	10	77	5·1	3	28	1,116
Eastern	690	748	11	112	7·7	3	24	1,023
South-Eastern	583	660	3	83	6·6	17	26	827
South-Western	857	68	4	28	3·02	—	3	107
North-Western	531	821	10	101	7·4	1	40	911
North-Eastern	82	23	4	5	4·7	—	1	49
Brook	133	91	—	8	3·5	4	—	120
Northern	38	404	4	7	1·5	2	—	423
Gore Farm	26	55	2	8	9·8	2	2	70
	4,052	4,885	68	607	6·7	66	131	5,851

This table gives the number of cases examined in which diphtheria bacilli were found. It also shows a small number of cases which were unsatisfactory at the first examination from a bacteriological point of view, but which clinically were undoubtedly diphtheria. Including those cases unsatisfactory from a bacteriological point of view and those from a clinical standpoint, there are about 5 per cent. of cases in which the bacteriological examination failed to assist in the diagnosis.

It will thus be seen that in the three years, out of 12,173 cases, diphtheria bacilli were found at the last examination in no fewer than 4,052, or 33·28 per cent.; and if we note the figures for the different years, we find that

In 1894 there were 25 such cases out of 45, or 55·5 per cent.

In 1895—1,594 such cases out of 5,296, or 30·1 per cent.

And in 1896—2,433 such cases out of 6,832, or 35·6 per cent. with the specific organism still in the throat at the last examination, and although it would be unfair to assume that all these cases had bacilli in their throats when discharged from hospital, yet doubtless in a fair proportion of the cases there can be no question that the organism was present, ready to be transmitted to those to whom the patient might come in contact. Bearing in mind the prevalence of diphtheria in London, and the fact that diphtheria can readily be transmitted by patients apparently well, this point would appear to have great importance from the danger to which such cases may expose the public.

From this table also another practical point may be observed. It will be noted that there were a certain number of cases in which bacilli were not found at the first examination, but were demonstrated subsequently. From this it must be concluded that the diphtheria bacillus, though present, was overlooked. Occasionally infection may have taken place after the first examination, and a subsequent examination confirmed the diagnosis, but the importance of making more than one examination is demonstrated in all cases where a doubt exists, especially in those where a negative bacteriological diagnosis is given.

There exist differences of opinion as to the influence on the course of the disease of different forms of diphtheria bacilli when present alone or in combination with streptococci and staphylococci. As regards the diphtheria bacillus alone, the highest mortality appears to be associated with the long bacillus, and in cases of mixed infection the most fatal form occurs when the bacillus is associated with the streptococcus group. The short bacillus would appear usually to have such slight virulence that it merely gives rise to a mild attack of sore-throat, but we must be careful to guard ourselves against the assumption that such

cases do not contain specific infection, or that the throats in which they are found are not sources of infection ; but in 148 cases in which the short bacillus was alone found there were only five deaths.

In all cases it appears that mixed infections give rise to graver lesions than simple infections, even with the most virulent form of diphtheria bacilli.

TABLE XIV.

Showing cases for 1895 *and* 1896 *in which no diphtheria bacilli were found after repeated examinations.*

Hospital.	Cases examined on 1	2	3	4	5	6	7 occasions.	Total Examinations.	Total Cases examined.	Percentage of whole of Cases examined.
Fountain - -	353	165	58	19	3	1	1	961	600	26·7
Western - -	432	76	12	4	—	—	—	636	524	26·08
Eastern - -	453	166	24	3	—	—	—	869	646	30·9
South-Eastern -	396	91	6	1	—	—	—	600	494	28·4
South-Western -	192	51	6	—	—	—	—	312	249	21·2
North-Western -	220	113	19	6	1	—	—	532	359	20·9
North-Eastern -	148	11	1	—	—	—	—	173	160	60·3
Brook - -	31	16	5	2	—	—	—	86	54	19·4
Northern - -	116	12	1	1	—	—	—	147	130	22·7
Gore Farm - -	11	8	1	—	—	—	—	30	20	19·8
Total - -	2,352	709	133	36	4	1	1	4,346	3,236	26·5

From this table it will be seen that in 3,236 cases, or 26·5 per cent. of the total cases examined during the two years 1895-96, no diphtheria bacilli were found, so that even allowing for errors of observation, over 20 per cent., or some 3,000 cases, were admitted to the Asylums Board's hospitals which offered no evidence, clinical or bacteriological, of diphtherial infection. The importance of these observations cannot be overstated, if only from the point of view that beds are occupied which could more properly be filled by genuine cases of diphtheria.

In that most fatal form of diphtheria, viz., hæmorrhagic diphtheria, the long and irregular forms of diphtheria bacilli were demonstrated in the throats of the patients, and in a large proportion of the cases there were staphylococci present either alone or in combination with the streptococci.

As a result of the observations made, the persistence of the diphtheria bacillus for periods up to eight weeks was of common occurrence, whether treatment by antitoxin was adopted or not, whilst the majority of cases seemed to retain bacilli in the throat from two to nine weeks. After the ninth week the number appears to fall very rapidly. In the year 1895 two cases were found to have the infective bacillus present beyond 200 days—in one of these antitoxic serum was used; and a considerable number remained infective beyond 100 days.

In 1896 no cases were found in which diphtheria bacilli were present after the 189th day amongst the injected cases, and after the 169th day amongst the non-injected cases. Ninety-four still contained bacilli on the mucous membranes after the 100th day amongst the injected cases, and 54 amongst those in which antitoxin was not given.

LECTURE II.

We have now considered the distribution of diphtheria and the connection of a specific micro-organism with the disease. To-day therefore I think we can conveniently study a few of the questions connected with its spread.

In the first place let us have a clear idea of the meaning of the terms "infection" and "contagion."

Infection was recognised by pathologists long before the advent of the knowledge of bacteriological causes for infectious diseases, but consequent upon this knowledge it is necessary to bring the phrase into line with our modern views. Formerly infectious diseases were considered to be those caused by certain poisons either entering the body from without or manufactured from within. To the latter the term "contagion" was applied, to the former "a miasma" was ascribed, the one arising within, the other outside the diseased organism. In accordance with this view the one class of diseases was transmissible from man to man, or man to animals, or animals to man, whilst the second class was acquired by means other than contact with similarly affected persons. This distinction gave rise to many difficulties, as may be shown by the single reference to anthrax or wool-sorter's disease, a disease communicable alone to man from animals suffering from the disease, but arising in animals without previous contact with similarly affected animals.

In the present day only such diseases are considered infective as are produced by a living organism entering the body from without, and capable of multiplication within.

A disease caused by a substance not capable of multiplication

within, such as a chemical body, is spoken of as an "intoxicative" process.

In such infectious diseases as diphtheria, anthrax, or tetanus, we have a combination of these two causes—viz., the mechanical presence of a specific organism, and the metabolic products of the life of such; indeed, the general rule of an infective process, due to a vegetable micro-organism, is that the principal lesions are occasioned not directly by the organisms, but indirectly by such organisms consequent upon the metabolic products of their growth. The difference between infection and intoxication is therefore at once apparent; the effects of the one are immediate, those of the other are only manifest after an interval. In the second case we have an interval, an incubation period, during which the poison is manufactured, and this interval varies according to the disease, being either short or long; the shorter the interval, the more closely the disease approaches an intoxication.

Sometimes the organisms produce mechanical disturbances either locally or generally, which are likely to materially modify the symptoms caused by the toxins. The intoxication may be local or general, examples of which are found, of the one in some forms of suppuration, and of the other in diphtheria.

The length of the incubation period in any given disease, and in any given person, is obviously most difficult to determine. But in the case of diphtheria the period is apparently short, and as a rule does not exceed two to three days. Contagion may be direct or indirect: it may be occasioned by contact—using the word in its widest sense—from body to body, or through the agency of a third body; in the one case, to prevent contagion, the infected body must be destroyed or removed, and in the other the infecting body, or the intermediary, or both, must be destroyed or removed.

Several of our infective diseases are occasioned by organisms capable of multiplication outside the body. These are seldom directly, or even indirectly, contagious. Cholera may be quoted as an example, sudden outbreaks of this disease being explained by the supposition that large numbers of the germs grow concealed and *unsuspected* outside the body, and that, becoming diffused through some general source of infection, such as the

drinking water, they gain access to the body; and it is further asserted that if an organism be widely distributed in space, contagion may be neglected as a means of spread, and the familiar instance of tuberculosis is quoted.

Closely associated with this aspect of the subject is the question of predisposition or susceptibility to disease. This may be either natural or acquired. Thus guinea-pigs are extremely susceptible to tuberculosis, man to diphtheria; on the other hand, man or animals may be naturally resistant to diseases, as is the hen to tetanus, in which case the resistance is absolute, whilst it may be only partial, as in the case of man to tuberculosis. Predisposition depends on various factors, the most important being intrinsic cell properties and extrinsic conditions reacting harmfully on the body and its tissues. Every organism to some extent has a power of resistance, in the form of special cellular mechanisms, to guard against infection. In diphtheria, for example, Loeffler has shown that the age and nature of the epithelial lining of a mucous membrane are conditions of great importance.

We know also that animals possessing the power of resistance to the contraction of certain diseases may be rendered susceptible by the adoption of certain measures; *e.g.*, pigeons and hens, which are naturally resistant to anthrax, can be rendered susceptible by starvation, whilst white rats do not in this way lose their immunity. The deprivation of water will also render dogs, hens, pigeons, and other animals susceptible to anthrax.

Again, fatigue, loss of blood, an unsuitable diet, exposure to heat, cold, or damp, are also capable of removing the natural immunity of animals. And what is true of individuals is also true of races. Negroes rarely suffer from yellow fever; black dogs contract anthrax more easily than white dogs, black and grey rats are less susceptible to anthrax than white rats; field mice readily contract tuberculosis, whilst white mice are practically immune.

Age also is an important factor. I shall have to show presently that in diphtheria the child is more susceptible than the adult. Closely allied with the subject of predisposition and natural resistance or immunity is that of acquired immunity. It is

impossible in the short space at my disposal to say much about this ; but it is common knowledge that if a person has suffered from an infectious disease, he is more or less protected against a second attack. In some cases the immunity is permanent, as with small-pox, whooping-cough, etc. ; in others it is transient, as with diphtheria. This is Nature's method by which the body is endowed with the power of resisting infectious diseases, and it is the basis of the scientific principles which, as I shall presently have to show you, are at the root of our modern methods of treatment. In the laboratory immunity may be produced by inoculation either with an attenuated virus or with small doses of living and fully virulent organisms, or thirdly, with the metabolic products or toxins of living bacteria. For this chemical vaccination either small doses of the virulent poison or of the attenuated toxins are used, and by repeated inoculation the animal is accustomed to withstand larger doses. In this way a tolerance of the poison is effected, so that if a sub-lethal dose of the toxin is first carefully and persistently employed, the animal soon becomes resistant ; and once the animal is rendered proof against the lethal dose, we may proceed more expeditiously.

Further experiments on this most interesting subject resulted in the proposition established by Behring that, " if an animal has been artificially protected against a particular infective agent, its blood or serum acquires the power when injected into another animal of directly transmitting an immunity from that agent " ; *e.g.*, the blood serum of animals artificially protected against diphtheria has the power of protecting susceptible animals both from infection by the diphtheria bacillus and from its toxin. It was further shown by Behring that the protective serum can exert this marvellous power even after infection has taken place, when the symptoms of infection or intoxication have set in, and consequently such serum is not only protective, but curative. It is obvious, however, that in this latter case larger doses of the serum and promptness in its application are desirable. If immunity be obtained by injections of the bacilli or its toxins, it is only subsequent to a struggle on the part of the animal with the disease. On the other hand, if serum be

injected, the part played by the animal is a passive one, there being no struggle whilst the immunity-conferring substance circulates through its tissues. Thus we have, according to Ehrlich, active and passive immunity. The changes which occur in the body to bring about this immunity it is not our province to follow; but it is interesting to note that Grohmann and Fodor have shown that the blood and normal tissue fluids possess marked antimicrobic properties, and Behring and others that, speaking generally, the blood serum of naturally immune animals does not possess any or but slight anti-microbic or protective properties.

There are several points in connection with the etiology of diphtheria which we shall now do well to study. I have already referred to the distribution of the disease in this and other countries as evidenced by the mortality maps, etc., which I placed before you in my last lecture.

By a reference to the charts, showing the school holiday periods, which give the weekly notifications of diphtheria in London, we find that the disease is most prevalent in the latter half of the year, and particularly in the last four months.

There is an interesting fact in connection with the age incidence to which perhaps I might here allude: it is that the two sexes are differently affected at the same age periods by diphtheria. In the first year of life boys are much more liable than girls to die of the disease; but this extra liability diminishes year by year, and in the third or fourth year it is transferred to the female side. This is true both in London and in the other parts of the country, as will be seen from the following figures, which are compiled from the Registrar-General's last seven annual reports.

Table I. shows the number of deaths from diphtheria among males and females at ages below 10, both for London and for England and Wales, during the seven years 1891-97.

Table I.

Deaths from diphtheria under ten years of age in the seven years 1891-97.

		Age.						
		Under 1 year.	1-2.	2-3.	3-4.	4-5.	Total 0-5.	5-10.
London	Males	530	1,422	1,385	1,316	1,087	5,740	1,810
	Females	461	1,255	1,299	1,372	1,221	5,608	2,380
England and Wales, excluding London	Males	1,084	2,297	2,379	2,800	2,630	11,190	5,171
	Females	857	2,128	2,358	2,820	2,560	10,723	6,130

It will be noticed that in London the maximum male mortality is at age one, the female mortality steadily increasing for the next two years, whilst in the remainder of the country a maximum is reached for both sexes at age three. But London and the remainder of the country are alike in this, that more females than males die from diphtheria at age 3, and many more in the age-group 5 to 10. It might be thought that these differences could be accounted for by the facts: (1) That more males than females are born; and (2) that the general mortality among males is greater year by year than that among females. Thus the excess of *male* mortality in the earlier years might be accounted for by the larger number born, and the excess of *female* mortality in the later years by the larger number of survivors. Reference to the census report shows, however, that this explanation is inadequate. After making due allowance for the different numbers of the two sexes living at each age, the following figures (Table II.) show the percentage which the female mortality from diphtheria bears to the male mortality *in equal numbers living at each age:*

TABLE II.

Percentage of female mortality to male mortality in equal numbers living at each age.

	Age.					
	0-1.	1-2.	2 3.	3-4.	4-5	5-10.
London - -	86·8	87·3	96·9	101·9	111·7	130·1
Remainder of England and Wales - -	77·6	91·5	97·8	99·8	96·6	118·0

In London the female mortality from diphtheria under one year of age is 86·8 per cent. of the mortality among an equal number of males at the same age. The percentage increases year by year, until at ages 2 and 3 the mortality of the two sexes is practically equal. After this the female mortality is in excess, being 30 per cent. more than the male mortality in the age-period 5 to 10. In the remainder of England and Wales the female mortality is only 77·6 per cent. of the male mortality under one year of age; but, as in London, the percentage increases year by year, except for a small irregularity at age 4, and the excess at age 5 to 10 is strongly marked, although it is not so great as in the case of London.

The age period 5 to 10 may be taken as very fairly representing school age; and any explanation of the incidence of diphtheria in London must deal with the fact that at this age girls are *one-third* more liable to die of diphtheria than are boys. It is hardly suggested by anyone that school aggregation increases the amount of diphtheria by so much as one-third; but here there is direct evidence of some influence or condition which either affects girls only, raising their diphtheria mortality by one-third, or else affects girls more than boys, raising the mortality of both, but raising that of girls enormously more than that of boys. No difference of the school conditions of the two sexes can be imagined which would yield even a plausible explanation. The cause must be sought among conditions affecting boys and girls in different ways or to a different extent, *outside* the schools.

It is interesting to notice that the same rule holds good when we consider notifications in London, the only difference being that the year of transference is in most cases a year earlier. (Table III.)

TABLE III.

Diphtheria notifications in London.

		Under 1.	1-2.	2-3.	3-4.	4-5.	
1891	M.	31	92	128	137	155	Female greater than male at every subsequent age.
	F.	28	88	114	149	167	
1892	M.	86	203	242	275	316	Ditto.
	F.	75	186	237	340	319	
1893	M.	118	378	449	513	520	Ditto.
	F.	113	288	437	531	545	
1894	M.	124	325	399	532	471	Ditto.
	F.	89	299	421*	548	503	
1895	M.	152	377	445	533	510	Female greater at every subsequent age except 9-10.
	F.	103	317	382	563	533	
1896	M.	131	424	572	712†	691	Female greater than male at every subsequent age.
	F.	115	363	507	645	749	
1897	M.	140	382	540	658	577	Ditto.
	F.	132	365	509	638†	673	
1898	M.	135	361	430	597	632	Ditto.
	F.	102	311	459*	541†	615†	

To test the *incidence* of diphtheria on children of various ages in London (apart from the *mortality*, which is compounded of the incidence and the case-mortality the latter of which may possibly vary largely at different ages) the actual notifications of the disease were ascertained for as many years as possible, in separate years of age up to 10 years, and for the ages 10 to 15 in one group. Unfortunately, the ages were so imperfectly returned in the years prior to 1892, as to make the figures useless for any purpose of comparison. In 1892, 1893, and 1894, however, the ages were stated in 95 per cent., 97 per cent., and 98½ per cent. of the cases respectively. and since that time, 1895-98, they have each year been above 99 per cent. By assuming that the small residuum of unstated ages in each year should be divided out in the same proportions as the stated ages, a very close approximation to the truth is obtained.

The next process was to estimate the number of children of each age living in London in each year. The number of children at each age between 5 and 10 was calculated by interpolation by the method of finite differences, and the corresponding numbers

* Female greater than male—exceptional.

† In these cases the male excess continues rather later than usual.

living in each year since 1891 were estimated on the assumptions: (1) That the increase of population has been at the same rate since 1891 as between the censuses of 1891 and 1896; and (2) that the proportion of children of each age in the total population has remained the same as at the census of 1891.

The population and notifications thus ascertained were then placed side by side, and the number of notified attacks of diphtheria per 1,000 living at each age was calculated. The following table (Table IV.) shows these attack rates for London in each year 1892-98, and also the average of the 7 years.

TABLE IV.

Diphtheria notifications per thousand living at ages under fifteen in London 1892-1898.

Year.	Under 1 year.	1-2.	2-3.	3-4.	4-5.	5-6.	6-7.	7-8.	8-9.	9-10.	10-15.
1892 -	1·61	4·16	4·91	6·45	6·90	6·61	5·64	4·04	3·33	2·83	2·14
1893 -	2·13	6·90	8·80	10·59	11·22	10·52	8·98	6·70	5·48	4·60	3·62
1894 -	1·92	6·30	7·94	10·67	10·00	9·91	8·45	6·58	4·71	4·22	2·94
1895 -	2·26	6·89	7·87	10·66	10·53	9·65	8·29	6·05	5·11	4·06	2·97
1896 -	2·15	7·72	10·09	13·05	14·37	12·75	10·14	8·57	6·51	5·59	3·63
1897 -	2·36	7·27	9·79	12·32	12·36	12·59	9·97	8·49	5·86	5·02	3·60
1898 -	2·04	6·47	8·22	10·71	12·21	11·68	9.38	7·64	5·14	4·33	3·15
Average of 1892-98 -	2·06	6·53	8·23	10·63	11·08	10·53	8·69	6·95	5·16	4·38	3·15

The first noticeable point about these figures is that the greatest attack rate is generally at age 4 to 5; the next that the attack rates are nearly equal for the 3 years of age 3 to 4, 4 to 5, and 5 to 6, and that on each side of this period of 3 years the rates fall considerably. A closer examination shows that infants under 1 year of age are remarkably exempt, their rates being on the average only about two-thirds of the rates for children between 10 and 15 years of age, and less than one-fifth of the rates at age 4 to 5. This exemption, however, appears to cease on completion of the first year of life. If the notification returns may be trusted, the liability to diphtheria is three times as great among children between 1 and 2 years of age, and four times as great among children between 2 and 3 years of age, as it is among infants in their first year. A possible explanation of this remarkable difference is that diphtheria is often spread by children sleeping

together, and that young infants, by sleeping with their parents, escape this source of infection.

Direct infection from person to person is probably by far the most common cause of diphtheria, and it will be easy to understand that the presence of the organism in the throat of a discharged patient, or in an adult where but little trouble arises since his power of resistance is great, might under favourable conditions for transmission be a fruitful source of the disease.

Milk is undoubtedly a vehicle of diphtheria, and outbreaks of the disease have been frequently traced to this source; but whether the disease is transmitted by the cow through the milk or whether the latter is in all cases accidentally infected is by no means satisfactorily solved. The subject has been investigated with great care on behalf of the Local Government Board, and the evidence would seem to be insufficient to prove that milk can be specifically contaminated by cows suffering from this specific disease.

The disease does not appear to have any direct relation to defective sanitary conditions, although such conditions may lower the general power of resistance and give rise to throat complaints, which would provide a favourable soil for the bacillus to thrive upon if it should obtain access. In the same way dampness of the soil or of houses might predispose to the disease.

Dr. Newsholme has suggested a relationship between the rainfall and the outbreaks of diphtheria. His propositions are that in London there is no exception to the rule that diphtheria only becomes epidemic in years in which the rainfall is deficient; and though in some years the excess of diphtheria in dry years is but small, there are no instances of a succession of wet years in which diphtheria was epidemic.

"Diphtheria only becomes epidemic in years in which the rainfall is deficient, and the epidemics are on the largest scale when three or more years of deficient rainfall immediately follow each other. Occasionally dry years are unassociated with epidemic diphtheria, though usually in these instances there is evidence of some rise in the curve of diphtheritic death-rate. Conversely, diphtheria is nearly always at a very low ebb during

years of excessive rainfall, and is only epidemic during such years when the disease in the immediately preceding dry years has obtained a firm hold of the community, and continues to spread presumably by personal infection."

But of all conditions which exert an influence upon the spread of the disease, that of school attendance is supposed by many to be by far the most powerful and far-reaching. Let us look into this a little more closely. But before dealing with London, let us examine the evidence on this point which can be gathered from provincial and foreign towns.

In order to ascertain the opinions of the Medical Officers in charge of schools and health departments at home and abroad as to the influence of schools on the prevalence of diphtheria, and also to inform myself of the methods adopted by other cities than London to prevent a spread of the disease in schools, I caused a circular letter to be addressed to the Medical Officers of a large number of towns in England and of important cities on the Continent and in America.

Amongst others, replies were received from Dr. M. Pistor, of Berlin; Dr. Würzburger, of Dresden; Dr. Siegel, of Leipzig; Dr. Bertillon, of Paris; Dr. E. M. Hoff, of Copenhagen; Dr. Gosetti, of Venice; Dr. Chapin, of Providence, U.S.A.; Dr. Matson, of Pittsburgh, U.S.A. These were chiefly in the form of personal opinions based upon individual experience, which, as will be seen later, differed considerably. From a few towns mortality returns of diphtheria were given for the different age-periods, together with the ages of compulsory school attendance.

These figures will be dealt with first. From Dresden, Leipzig, and Vienna the number of deaths from diphtheria over a number of years at each age-period from 1 to 10 was furnished. Now, whilst there are objections to receiving death-rates as evidence of the prevalence of a disease, yet these are the only figures on the subject available for purposes of comparison, with the exception of London, where, owing to the notification system, far more valuable evidence is obtained from a consideration of the actual number of cases of illness.

Moreover, the number of deaths which have occurred at each

age is obviously useless as a comparison of the prevalence of the disease at different periods of life, on account of the varying number of individuals living at these ages. In the case of the above-mentioned towns, Dresden, Leipzig, and Vienna, it is impossible to obtain the age-distribution of the inhabitants. Consequently, in order to make use of the figures supplied, it was necessary to assume that the age distribution of each city was similar to that of London. There is obviously a very great objection to this assumption, and the following table (Table V.) is submitted, after this explanation, on the grounds that these are the only figures which can be obtained for the comparison of English with foreign towns:

Table V.

City.	Period from which the figures are drawn—inclusive.	Age of compulsory school attendance.	Mean annual death-rate per thousand from diphtheria at the different ages.									
			0-1.	1-2.	2-3.	3-4.	4-5.	5-6.	6-7.	7-8.	8-9.	9-10.
Dresden	1884-1894	7-14	2·99	9·03	9·3	9·71	6·45	4·81	3·44	2·38	2·13	0·96
Leipzig	1889-1897	6-14	1·92	5·88	6·68	5·56	4·83	3·29	2·48	1·91	1·75	0·73
Vienna	1887-1889	6-14	3·68	9·51	6·55	4·50	3·20	2·26	1·25	0·97	0·52	0·34

It will be seen from these figures, taking them for what they are worth, that the period of life on which diphtheria falls most heavily is during the first few years, and in this respect the result tallies closely with the figures obtained by more reliable methods for London. The years of greatest mortality in Dresden are the second, third, and fourth; in Leipzig the second, third, fourth, and fifth; and in Vienna the second and third; while in none of these towns is education compulsory till the sixth year, by which time the mortality has dropped considerably. Consequently, since the above figures, in spite of the assumption mentioned above, are probably not very far from the mark, it can be safely asserted that in these towns at least the chief risk of infection occurs previous to the school age.

From Paris, Copenhagen, and Venice the returns are not so full (Table VI.), but in each case the age of maximum mortality is considerably earlier than the minimum age of compulsory school attendance.

TABLE VI.

City.	Ages of maximum mortality.	Age of compulsory school attendance.
Paris - - -	1-3	6-13
Copenhagen -	2-3	7-14
Venice - -	1-2	6 and upwards.

The opinions regarding the influence of compulsory school attendance on the spread of diphtheria, which have been formed by the various authorities above enumerated, differ considerably in the different localities. On reading through their statements, however, the impression obtained is that the majority consider attendance at school to be an unimportant factor in the spread of the disease; that it undoubtedly plays a small part, but no greater than would occur wherever social intercourse can take place; and, more important still, that closure of schools and abolition of compulsory education would not stamp out the disease.

I may here take the liberty of quoting in this connection extracts from the reply courteously supplied by Dr. Charles V. Chapin, Superintendent of Health, of Providence, U.S.A.:

"As to the relation of diphtheria to school attendance, it appears to me that it is not very close . . . I do not believe that if the schools were closed during the year there would be a great falling off in diphtheria. We certainly have fewer cases of diphtheria during the long summer vacation, but I take this to be due to the unfavourable influence of hot summer weather upon the propagation of the disease. My reason for this view is based on the fact that diphtheria usually drops off in the spring, and is very decidedly diminished in June, while the schools remain in session till July. The long vacation extends from July 1 to the end of the first week in September. Furthermore, it appears to me that if diphtheria was largely spread through school attendance, we should very often find local epidemics confined to a single school, but such is rarely the case in this city."

Similarly Dr. E. G. Matson, Pittsburgh, U.S.A., says:

"Whoever expects to suppress diphtheria by closing the schools should also take measures to confine children to houses. Although it is possible to a large extent to prevent infected

children from attending school, it is impracticable to keep them out of the streets. For this reason children at school may be actually in the place of least danger."

Whilst Dr. Bertillon, of Paris, says:

"It seems to me that every assemblage of children facilitates the propagation of diphtheria. It is evidently impossible to prevent children—and especially the children of the lower classes—from assembling. If they are not sent to school they will assemble all the same to amuse themselves. In this case there will be no supervision, and there will be greater opportunity for them to infect one another than if they were in a school. In the second case they are under supervision, while in the first case they are not. . . . Of all the opportunities that children have of assembling together, that which school affords them appears to me the least dangerous."

With regard to opinions received from the other towns, it may be mentioned shortly that the Medical Officers of a large number of cities and towns, such as Birmingham, Bradford, Greenock, Aberdeen, Dresden, Leipzig, Copenhagen and Venice, considered that on the whole there was no important causal relation between schools and diphtheria.

But to return to London.

It has been stated by Mr. Shirley Murphy that "the diphtheria mortality at ages 3 to 10 years did not fall in 1871-80 in anything like the same degree as the diphtheria mortality at all ages"; that "this new departure is most notable in London"; that "it is suggestive of a fresh factor of diphtheria at ages 3 to 10 years becoming operative in the decennium 1871-80"; and that "as regards England and Wales and London in 1881-90, as compared with 1861-70, the special incidence on the age 3 to 10 years is practically maintained."

Now it may at once be freely admitted that if it were true to say—

(*a*) That children aged 3 to 10 years attend school, and children under 3 years of age do not;

(*b*) Further, that diphtheria has of late years increased greatly amongst children aged 3 to 10 years, whilst children under 3 years of age have been comparatively exempt—

then, undoubtedly there would be a very strong presumption that school attendance is the chief cause of the increased incidence of the disease. But are these statements correct? In order to test this, it is not enough to begin by grouping the facts under the ages 0 to 3 and 3 to 10; it is necessary to ascertain what is the age-grouping under which each set of facts most naturally falls. For instance, if it were found that the age of school attendance practically begins at 4 years, and that the special liability to diphtheria begins at 2 years, there could be hardly a doubt that the two things are independent. In such a case, the age-grouping 0 to 3 and 3 to 10 would only suggest false conclusions.

Turning therefore to the evidence to be obtained from the returns for London, we are on much safer ground, since we are no longer dependent on mortality figures, but can make use of the notifications, and therefore the incidence of the disease, which yields far more reliable evidence.

The *average* numbers of children at various ages on the rolls of the London School Board in the seven years 1892-98 were as follows:

TABLE VII.

Average number of children at various ages on the roll of the London School Board, 1892-98.

Under 3 years	352
3 years and under 4	13,702
4 ,, ,, ,, 5	31,454
5 ,, ,, ,, 6	49,049
6 ,, ,, ,, 7	54,624
7 ,, ,, ,, 8	56,481
8 ,, ,, ,, 9	54,669
9 ,, ,, ,, 10	55,684
10 ,, ,, ,, 11	55,372
11 ,, ,, ,, 12	53,332
12 ,, ,, ,, 13	48,813
13 ,, ,, ,, 14	25,413
All ages under 14	498,945

The average number of children in London living at age 3 to 4 may be taken as about 143,000; so, obviously, a very small proportion of children at this age are subject to the risk of school infection, and it is more correct to speak of 4 years instead of 3 years as the age at which school attendance commences. We should therefore expect that any tendency to school infection would show itself in a marked manner at age 4.

Turning again to the table (Table IV.) showing the diphtheria notifications per 1,000 living at ages under 15, it is seen that the greatest number of attacks take place between the ages of 3 and 6, and that there is a marked drop after this age.

The same argument which has been used above, in respect of the increase or decrease of diphtheria mortality at particular ages in successive periods of time, is applicable to these notification rates, viz.: if it can be said (1) that children above a certain age attend school, while those below that age do not, and (2) that children above that age are specially subject to diphtheria, while those below it are comparatively exempt—then there will be a strong presumption that school attendance is the main factor in the spread of the disease. This point is so important that it is desirable to present it in the clearest possible manner. Two diagrams have, therefore, been prepared, the first of which shows the average number of children on the roll at each age under 10 years in the seven years 1892-98 inclusive, while the second shows the average number of diphtheria notifications at each age under 10 in the same period. As the number to be represented in Diagram I. exceeds 50,000 at the maximum age, while the notifications scarcely exceed 1,100, a uniform vertical scale for the two diagrams would have been inconvenient. Accordingly, the vertical scale of Diagram II. has been made ten times as great as that of Diagram I.

A glance at the diagrams shows at once that the conditions just suggested do not exist. It is true that the notifications reach their maximum at ages 3 to 5, the first years in which any appreciable number of children attend school; but they reach this maximum, be it noted, by a steady yearly rise through the ante-school period of life.

DIAGRAM I.

Average numbers of Children at each age under 10 years on the roll of the London Board Schools from 1892-98.

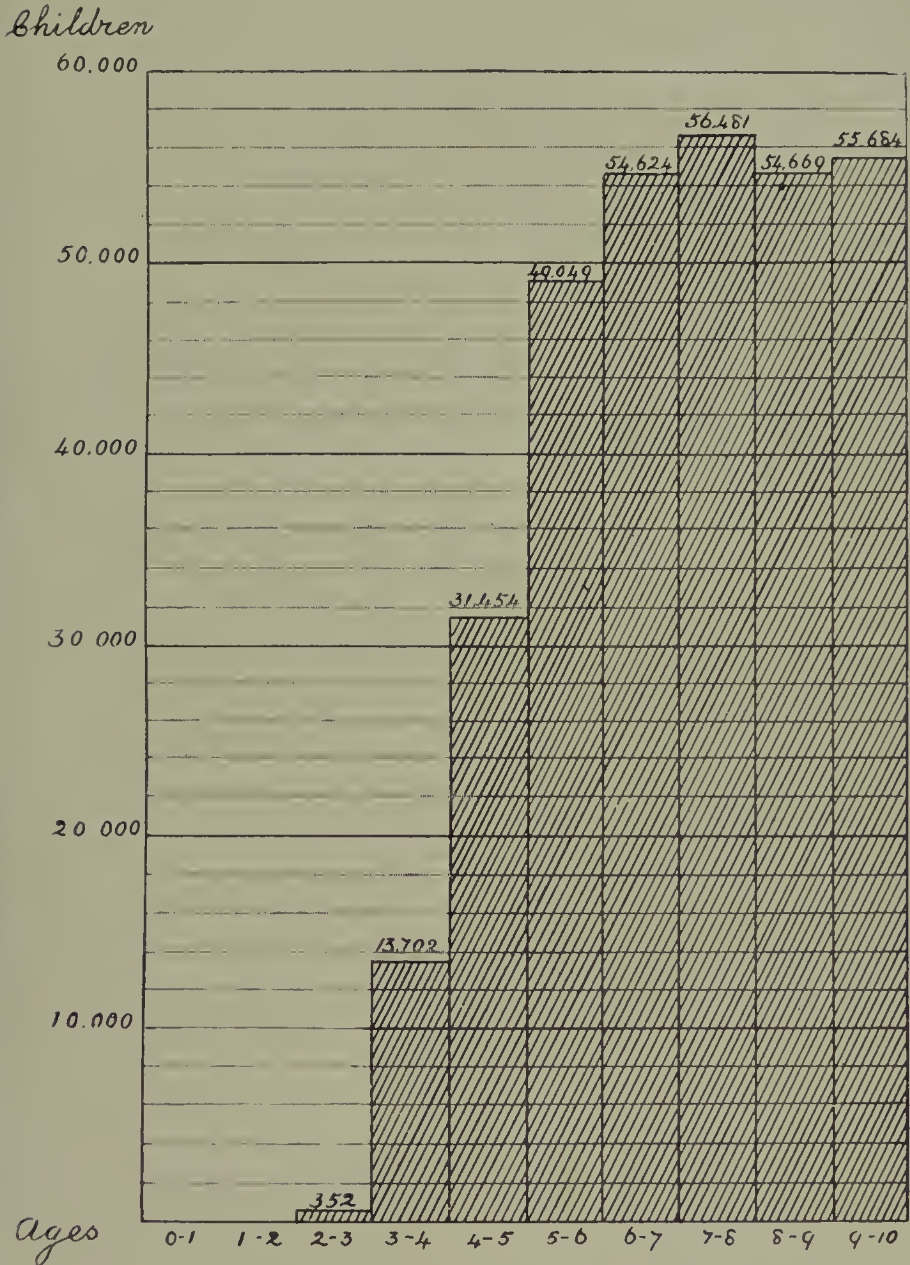
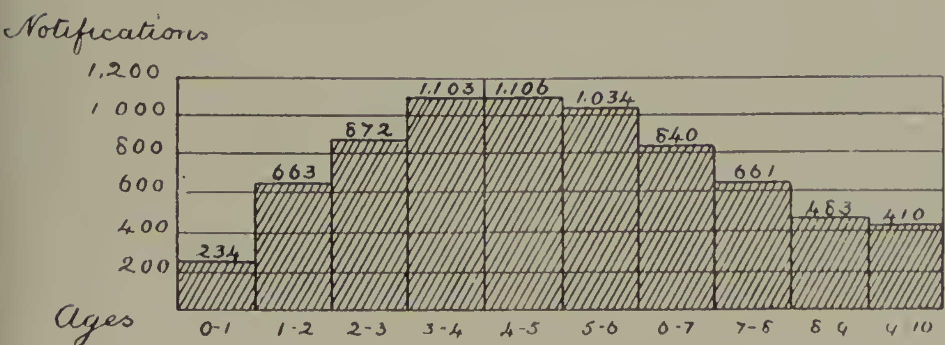


DIAGRAM II.

Average annual notifications of Diphtheria in London at each age under 10 in the seven years 1892-98.



At the age 4 to 5, although there are more than twice as many children attending school as between 3 and 4, yet the number of attacks is practically the same at the two periods; while from 5 to 6 the school-attending children are more than three and a half times as numerous as at the age 3 to 4. That is to say, greatly increased numbers of children are subjected to the risks of school infection, and yet the number of attacks is either the same or shows a decline.

Turning to the numbers themselves (which are printed at the tops of the columns in the diagrams), we find that the attacks at age 1 to 2 were nearly three times as many as in the first year of life. At age 2 to 3 they were 31·5 per cent. more than at age 1 to 2; and at age 3 to 4 they were 26·4 per cent. more than at age 2 to 3. Thus the *proportional increase* was less in the first year of nominal school life than in the year immediately preceding it. In the next year of age—4 to 5 years—an increase of 129 per cent. in the children attending school is accompanied by an increase of only ·3 per cent. in the diphtheria attacks; and at the age 5 to 6 a further increase of 55·7 per cent. in the children attending school is accompanied by a decrease of 6·5 per cent. in the diphtheria attacks.

Stronger evidence could hardly be adduced that age susceptibility is the main factor in the selection of the victims of diphtheria, and that, at the most, school aggregation acts only as a slightly disturbing element. It appears reasonable to suppose that if there were no school attendance at all, the increase of attacks at age 3 to 4 over age 2 to 3 might be somewhat less than 26 per cent., and that the decrease in subsequent years might be somewhat more rapid than it actually is. But this is only another way of saying that diphtheria is sometimes communicated at school; the age-incidence would probably be altered to a much greater extent if children were prevented from playing together out of school. Such suggestions are, however, entirely hypothetical. But it is a fact that a child becomes *more* liable to be attacked by diphtheria year by year as it approaches school age, and becomes *less* liable year by year after it has reached school age.

From the facts represented in these diagrams it is impossible to resist the conclusion that no *special increase of liability* to diphtheria can be traced to the beginning of school attendance. In fact, the ages which are now the most subject to the disease would still be the most subject if aggregation in schools were abolished altogether. It may, or may not, be that the decrease of liability would commence at ages 5 to 6, and would go on more rapidly in succeeding years than it really does, but the steady increase of liability at ages 1 to 2, 2 to 3, and 3 to 4, would remain practically unaltered.

Somewhat marked attention has been drawn to the fact that certain holiday periods in the schools of the Board have occurred simultaneously with a decrease in the notifications of diphtheria, and it is, consequently, by many assumed to have been proved that so-called school influence is the main factor in determining the spread of the disease.

I should not be prepared, without other evidence, to attach the importance which some are disposed to do to this point even if proved, but I think I can show there is nothing like constancy in the relationship of school holidays and a decrease in the notifications of diphtheria.

The accompanying charts, Nos. 1, 2, 3, 4, 5, and 6, 7, 8 and 9 show graphically the weekly notifications of diphtheria for the years 1890-98, with the holiday periods at the schools of the School Board for London marked by asterisks.

So far as chart 1 is concerned, there is absolutely no evidence of any relationship in 1890; it will be noted that from the twenty-eighth week to the thirty-first week there is a gradual rise in the number of notifications, the thirty-first week being the first week of the holidays; then there is a fall, but the amount of diphtheria for the next two weeks is above the mean for the year; and so it remains for the rest of the year, with a striking exception, viz., the fifty-second week, when there is a marked fall, which cannot be taken, however, in support of the school-influence theory, for the depression occurs a little too early, and in the following week, where we should have looked for a further decline, we find instead an actual rise.

CHART I.

Weekly Notifications of Cases of Diphtheria (excluding Membranous Croup) occurring in London in 1890.

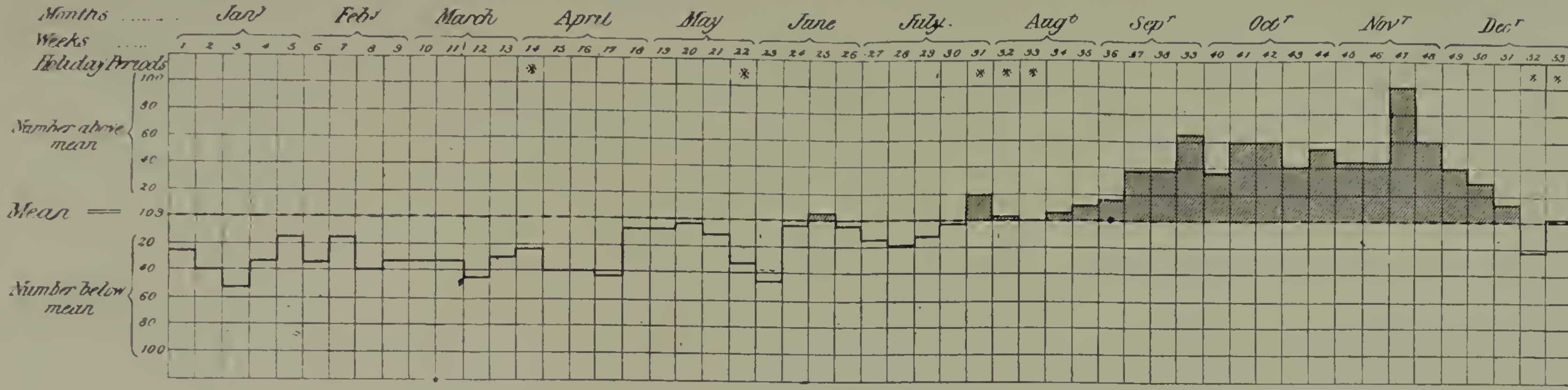


CHART II.

Weekly Notifications of Cases of Diphtheria (excluding Membranous Croup) occurring in London in 1891.

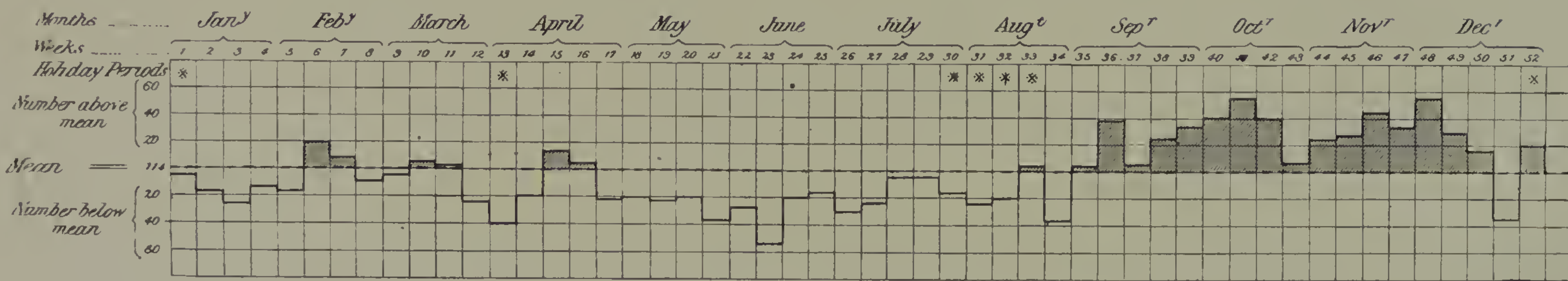


Chart III.

Weekly Notifications of Cases of Diphtheria (excluding Membranous Croup) occurring in London in 1892.

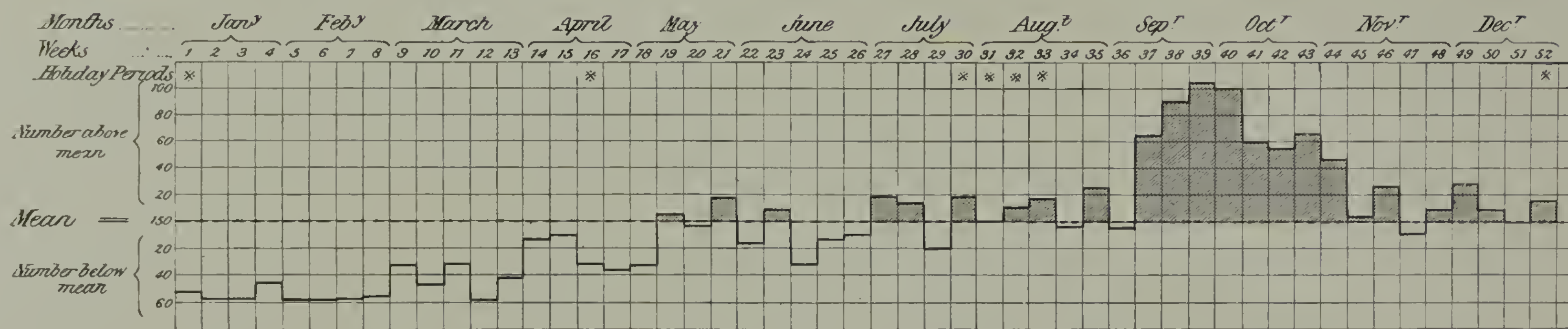
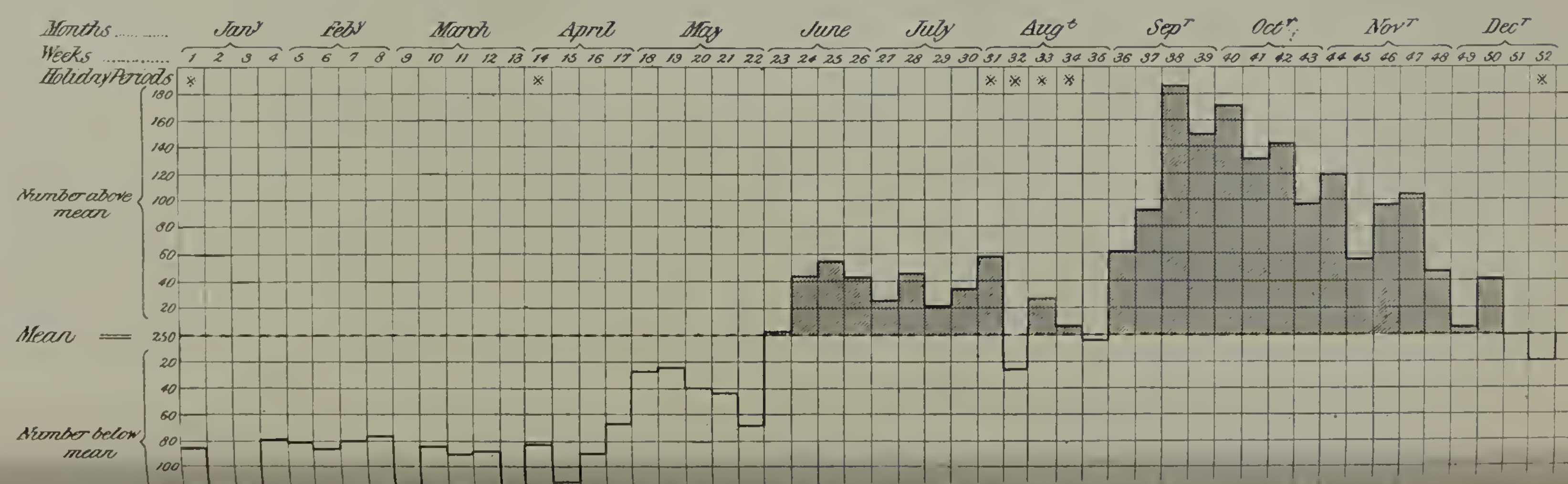


Chart IV.

Weekly Notifications of Cases of Diphtheria (excluding Membranous Croup) occurring in London in 1893.



Plate

Weekly Notifications of Cases of Diphtheria (excluding Membranous Croup) occurring in London in 1894.

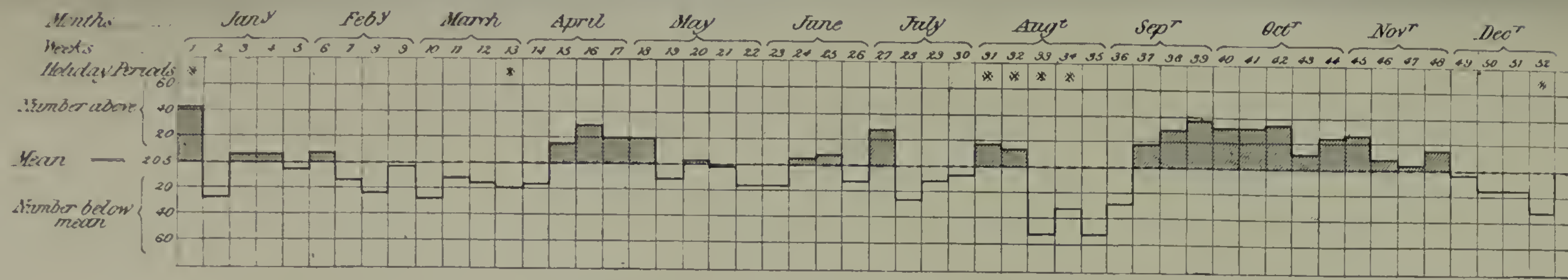


CHART VI.

Weekly Notifications of Cases of Diphtheria (excluding Membranous Croup) occurring in London in 1895.

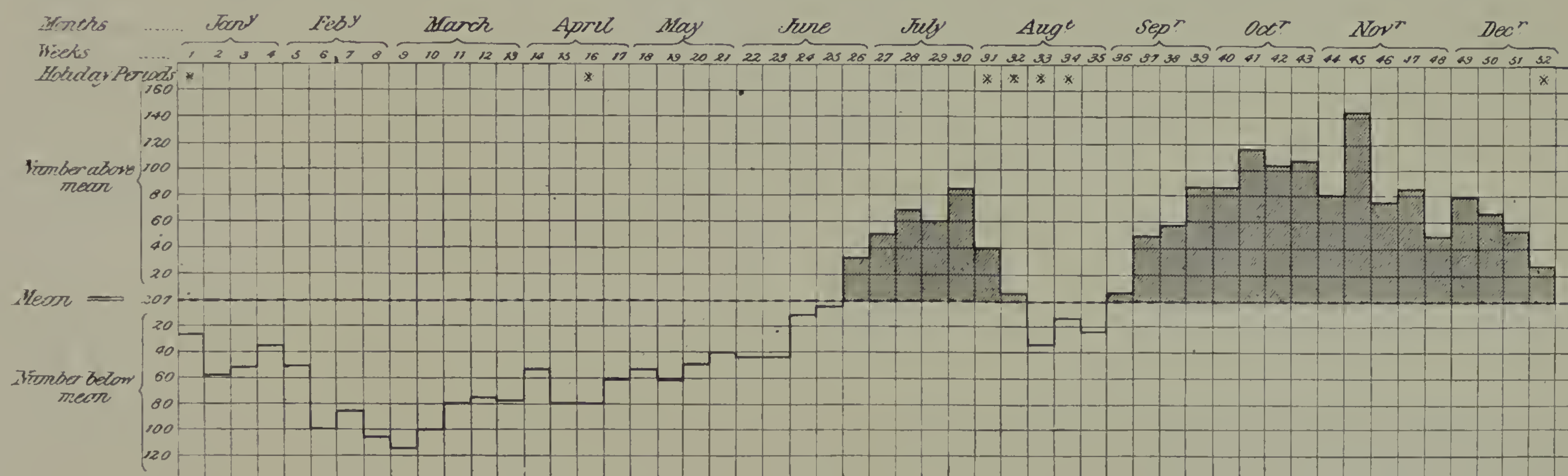


Plate XVIII

Chart 2 shows for 1891 much the same state of things ; during the twelfth and thirteenth weeks there is a fall in the curve. The latter being a holiday period, we naturally look, therefore, for a further fall in the fourteenth week, but we actually get a rise, and in the following, or fifteenth week, an increase above the mean for the year, and then from the sixteenth week for a period of three months, although the schools are in session and diphtheria is never absent, the incidence of the disease is for the most part well below the mean until the thirty-third week, or the last week of the summer holidays, when there is a sudden rise above the mean, followed in the first week of school work by a sudden fall, subsequent to which the usual seasonal incidence occurs, followed by a somewhat peculiar fall in the fifty-first week of the same character as that noticed in 1890.

The chart for 1892 gives no kind of support to the suggestion that in London a connection exists between the holiday periods and the incidence of diphtheria ; indeed, it will be seen that for the whole period of the summer holidays the amount of diphtheria was above the mean, whilst for the twenty-ninth week, or that immediately before the holidays, and for the thirty-fourth week, or that immediately after the holidays, it was below the mean.

And in 1893 there is evidently again no kind of connection, for during the first week of the summer holidays the notifications were more numerous than they had been previously in the year, and in the second holiday week there was a marked decline, followed, however, in the third week by a great increase, no possible school-influence being at work.

The curve for 1894 shows for the summer holidays during the first two weeks a place for the curve above the mean, the previous three weeks of school life being below the mean, and for the latter two weeks of the holidays and the first two weeks of school work the notifications are shown below the mean.

Chart No. 6 for 1895 at first sight appears to show that school-influence did in that year play a chief part in the spread of diphtheria. It will be noted that there is a marked drop in the number of notifications at the very commencement of the holidays, and that the notifications as suddenly rise on their termination. This raises

the question whether the drop during the holidays is really due to the closure of the schools or to some other cause. With a view of solving this question, a very careful analysis of the notifications has been made. The school holidays lasted from July 27 to August 24. Taking the notifications at each age, then, for the four weeks preceding the holidays, *i.e.*, the four weeks ending August 3—for school-influence would naturally not be manifested for some days after the closure of the school—and comparing them with the notifications during the four weeks of holiday, *i.e.*, the four weeks ending August 31, and also with those of the four weeks after the holiday, *i.e.*, the four weeks ending September 28, we get the following table:

TABLE VIII.

Notifications in London at each age for the four weeks before, during, and after the holidays in August, 1895.

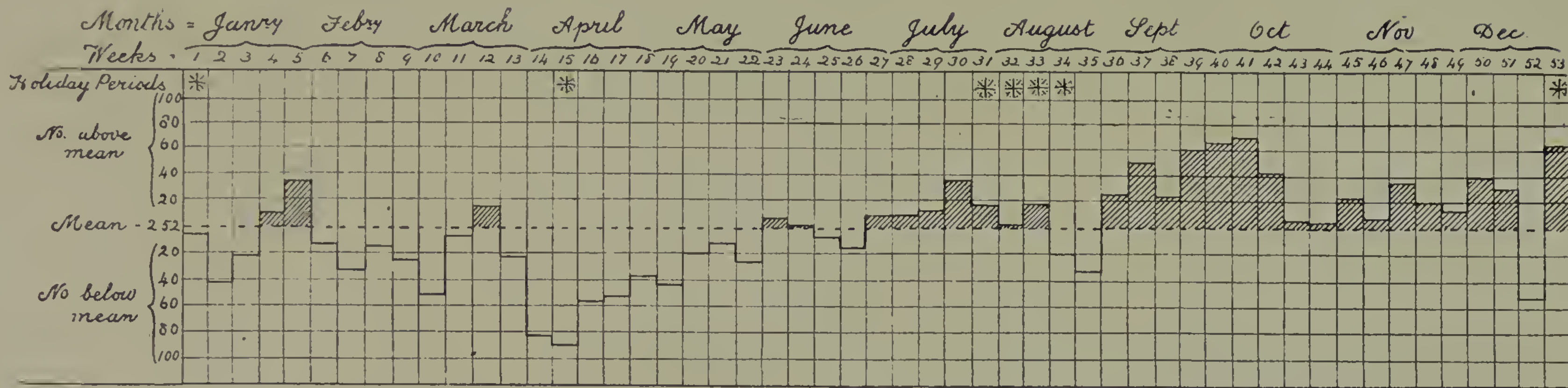
Four weeks ending—	0.	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.	13 to 15.	15 and upwards.
August 3 -	33	66	82	116	119	103	81	65	54	48	34	29	30	48	228
August 31 -	18	59	59	74	71	57	62	39	30	32	31	19	13	35	201
September 28 -	25	56	73	114	109	86	92	71	46	39	44	23	24	40	233

It is at once apparent that the drop in the notifications is almost as marked at the ages below school-age as at school-ages, and is also well marked at ages above school-age. The recrudescence after the holidays is also seen in the three groups of ages, though here the increase is most marked in children of school-age.

In these charts the notifications of diphtheria have alone been given, but in other countries croup and diphtheria are looked upon as one disease, and this is now the tendency in our own country. I have thought it well, therefore, whilst preserving the arrangement hitherto existing for the sake of continuity, to give for each of the years 1896, 1897, and 1898, a separate curve for the cases of croup; from these it will be seen that the numbers of cases are so small that even if they had been included in the diphtheria chart they would not have materially affected the curve; it will, however, be noticed that the croup curve does not always follow that of diphtheria; croup notifications appear to be more numerous in the winter and spring, and below their mean in the summer months.

CHART VII.

Weekly Notifications of Cases of Diphtheria (excluding Membranous Croup) occurring in London in 1896.



Weekly Notifications of Cases of Membranous Croup occurring in London in 1896.

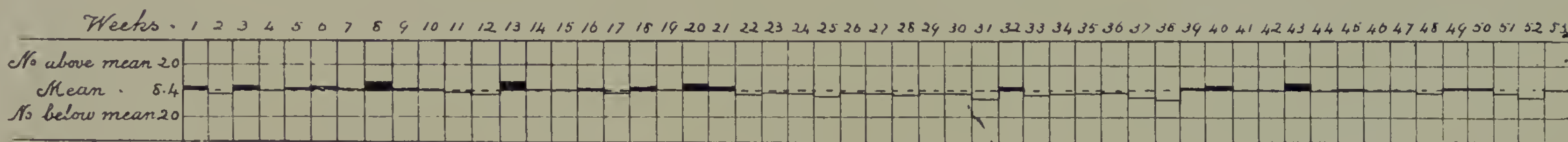
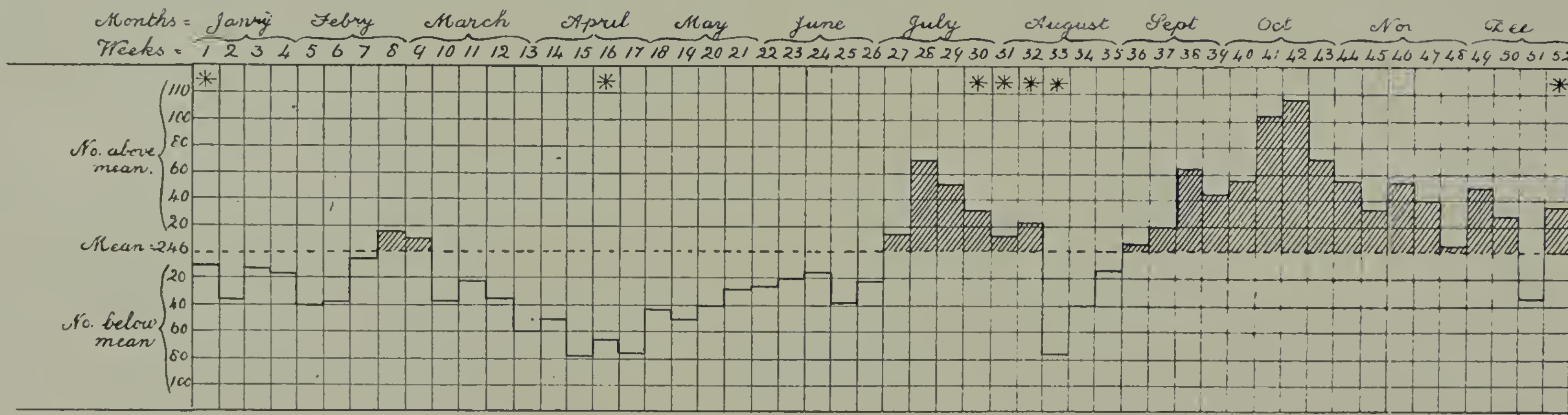


Chart VIII.

Weekly Notifications of Cases of Diphtheria (excluding Membranous Croup) occuring in London in 1897.



Weekly Notifications of Cases of Membranous Croup occurring in London in 1897.

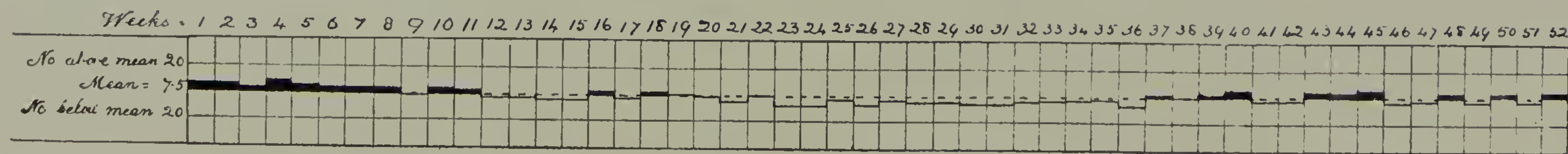
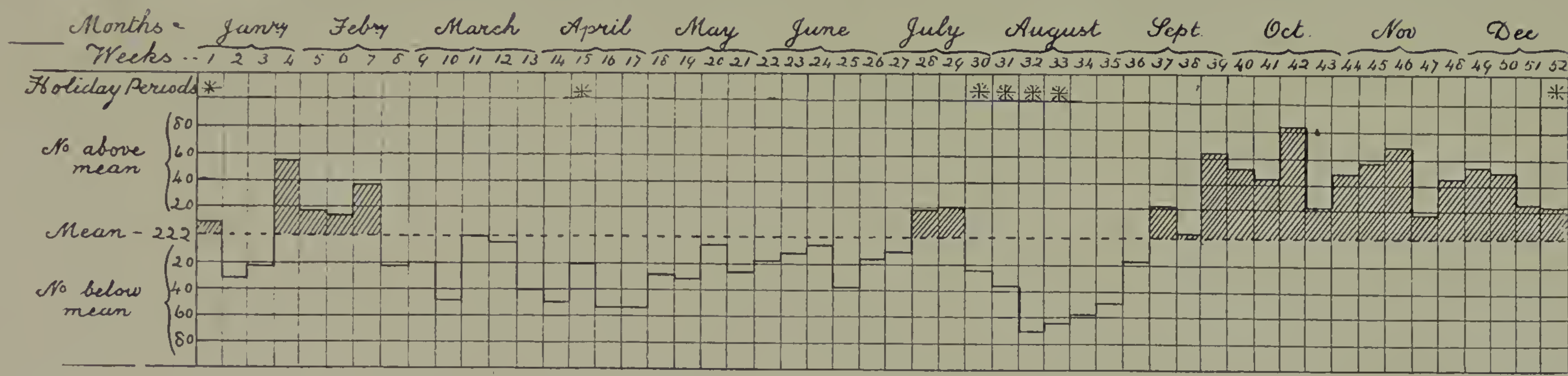
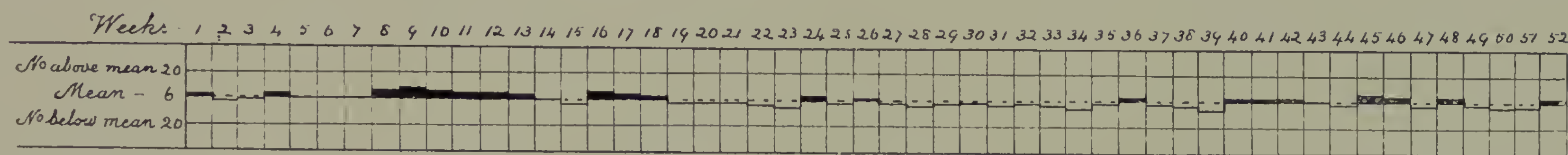


CHART IX.

Weekly Notifications of Cases of Diphtheria (excluding Membranous Croup) occurring in London in 1898.



Weekly Notifications of Cases of Membranous Croup occurring in London in 1898.



In 1896 the first maximum is less marked ; a slight fall occurs in the first week of the holidays, and is continued in the second, but the next week shows a rise, and for the three weeks the notifications are above the mean, for the two following weeks the notifications are below the mean, and then the usual autumn rise occurs.

In 1897 the holidays began in the thirtieth week, the first maximum number of cases occurred in the twenty-eighth week, and then for a period of three weeks there is a steady fall, interrupted by a slight rise in the third holiday week, and followed in the fourth week of the holidays by a low minimum from which a gradual rise takes place to the second maximum in the forty-second week.

There is a very peculiar fall in the fifty-first week, the week before the Christmas holidays, which is also to be noticed in the chart for 1896 for the same week.

I think it will be agreed that these two charts do not in any way show the marked connection suggested between the holiday periods and the number of notifications.

In 1898 the first maximum is very slight, consisting of a rise to twenty above the mean in the twenty-eighth and twenty-ninth weeks. The holidays begin in the thirtieth week, and coincide with a fall lasting three weeks. In the last week of the holidays the rise to the autumn maximum sets in.

From a consideration of these curves, I am at a loss to understand, if school influence plays the predominant part suggested, why we do not get a greater incidence of the disease during the many weeks the schools are in session, and when for the most part the curve is below the mean ; and I confess I should be inclined to attach greater weight to the coincidences if year by year we found a fall occurring with regularity in the first holiday week, and being maintained throughout the holidays ; but this is by no means the case.

The falls during the holiday periods may be accounted for by the smaller number of children at these times in London, and perhaps more fully by the removal of the supervision which is exercised by a staff of some 10,000 teachers in the Board Schools alone during school periods.

I append a table showing the notifications for the sanitary areas of London for a series of years.

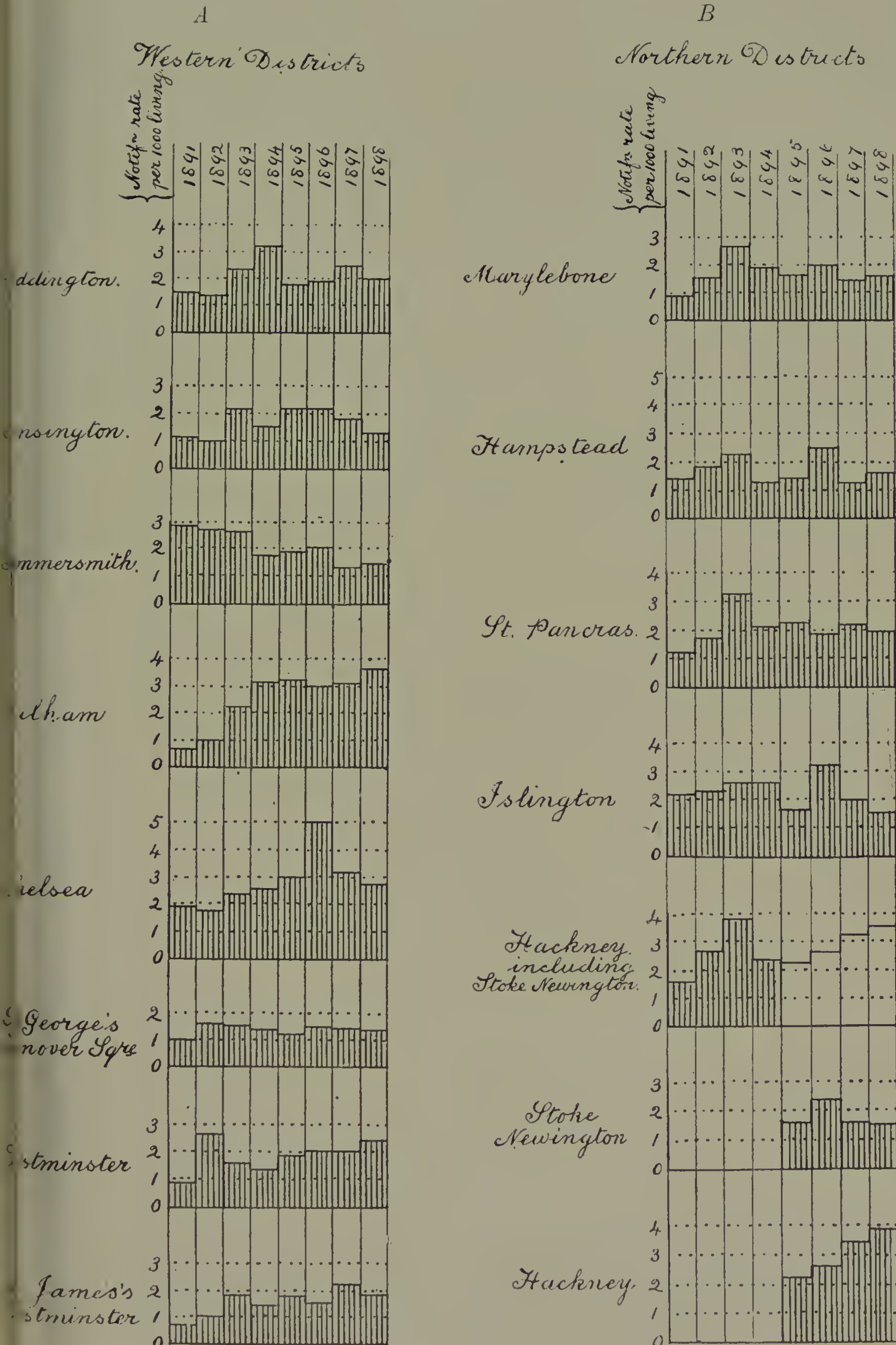
TABLE IX.

Local incidence of diphtheria in London in the years 1891 *to* 1898.—*Notifications per* 1,000 *of the estimated population in each sanitary area.*

Sanitary Area.	1891.	1892.	1893.	1894.	1895.	1896.	1897.	1898.
Kensington	1·11	1·04	2·14	1·61	2·18	2·12	1·88	1·25
Fulham	·71	1·03	2·21	3·15	3·21	2·97	3·15	3·71
Hammersmith	2·92	2·75	2·65	1·74	1·83	2·00	1·39	1·48
Paddington	1·53	1·43	2·32	3·11	1·86	1·91	2·49	2·01
Chelsea	1·80	1·74	2·31	2·56	3·06	4·98	3·16	2·77
St. George's, Hanover Square	1·03	1·56	1·53	1·37	1·22	1·54	1·49	1·36
Westminster	·88	2·57	1·48	1·33	1·90	2·00	2·07	2·38
St. James's, Westminster	·76	1·04	1·92	1·50	1·81	1·48	2·17	1·85
Marylebone	·98	1·53	2·75	1·96	1·68	2·02	1·55	1·65
Hampstead	1·48	1·89	2·20	1·29	1·46	2·56	1·35	1·69
St. Pancras	1·26	1·74	3·27	2·12	2·25	1·95	2·20	1·99
Islington	2·18	2·22	2·63	2·62	1·71	3·23	2·06	1·54
Stoke Newington	1·71	2·69	3·83	2·29	1·61	2·26	1·55	1·53
Hackney					2·25	2·67	3·47	3·89
St. Giles's	·63	1·51	1·90	1·11	1·51	1·47	1·43	1·07
St. Martin-in-the-Fields	·27	1·71	1·78	1·14	1·32	1·15	1·66	0·64
Strand	·44	1·11	3·11	1·14	1·72	1·51	0·94	1·93
Holborn	·93	1·83	2·91	2·02	1·64	2·23	5·21	4·80
Clerkenwell	1·84	1·72	4·25	2·35	1·96	3·54	5·21	3·96
St. Luke's	1·39	·99	3·48	1·44	2·20	3·11	4·48	4·53
City of London	·83	2·47	1·81	1·14	1·27	2·23	1·98	1·51
Shoreditch	1·71	1·63	3·92	2·29	1·89	2·86	2·89	2·01
Bethnal Green	2·15	4·12	5·46	3·92	3·34	3·29	3·94	2·49
Whitechapel	2·08	3·25	2·67	2·22	3·62	4·27	3·55	2·16
St. George's-in-the-East	1·95	2·75	5·14	4·33	4·75	4·37	3·82	2·18
Limehouse	1·18	1·39	4·01	3·20	3·25	4·52	3·25	2·28
Mile End	·97	2·31	3·17	3·03	4·33	4·86	3·87	2·47
Poplar	2·65	2·62	6·52	3·72	4·27	3·96	3·95	2·68
St. Saviour's, Southwark	1·25	1·44	3·17	3·20	2·44	3·24	3·85	4·64
St. George's, Southwark	·89	1·24	2·92	2·95	1·67	3·00	3·06	3·90
Newington	·85	1·30	3·86	2·57	2·19	3·19	2·59	3·66
St. Olave's, Southwark	·55	1·26	2·40	2·17	1·68	3·68	2·53	1·42
Bermondsey	·89	1·05	2·40	3·07	1·29	2·92	3·14	3·02
Rotherhithe	·82	1·09	2·50	3·60	3·31	2·89	1·99	1·00
Lambeth	1·21	1·80	2·75	2·13	2·21	2·24	2·42	2·65
Battersea	2·06	2·34	3·90	2·95	2·19	2·36	3·57	4·57
Wandsworth	1·08	1·52	2·42	1·92	1·42	1·57	2·88	2·93
Camberwell	·99	1·20	2·00	2·84	3·52	5·54	4·47	2·57
Greenwich	·91	1·04	2·74	3·28	4·93	4·65	3·31	2·98
Lewisham	·75	2·70	2·59	1·92	1·51	4·31	2·52	3·16
Woolwich	·20	·39	·62	1·17	1·56	2·42	3·57	2·63
Lee	·61	1·40	2·28	1·66	1·18	1·94	2·81	4·05
Plumstead					2·18	3·34	2·16	1·78
LONDON	1·42	1·85	3·02	2·44	2·45	3·02	2·87	2·56

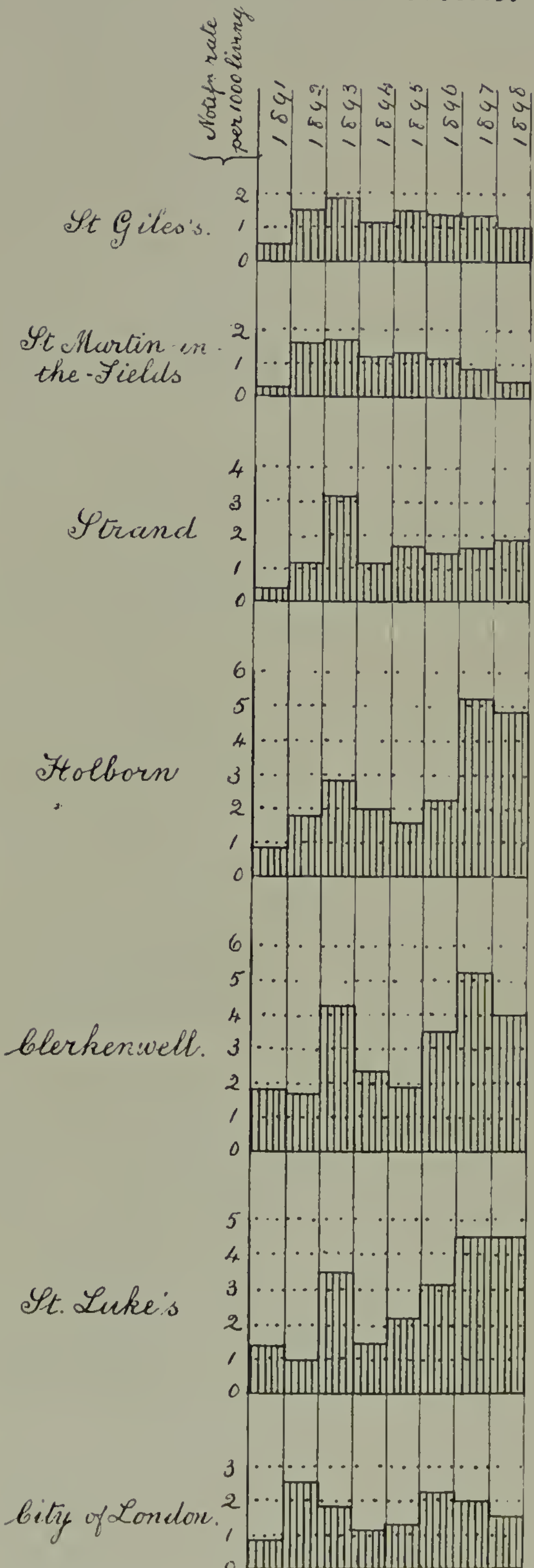
CHART X.

Diphtheria Notifications in the several Sanitary Districts of London per thousand living.



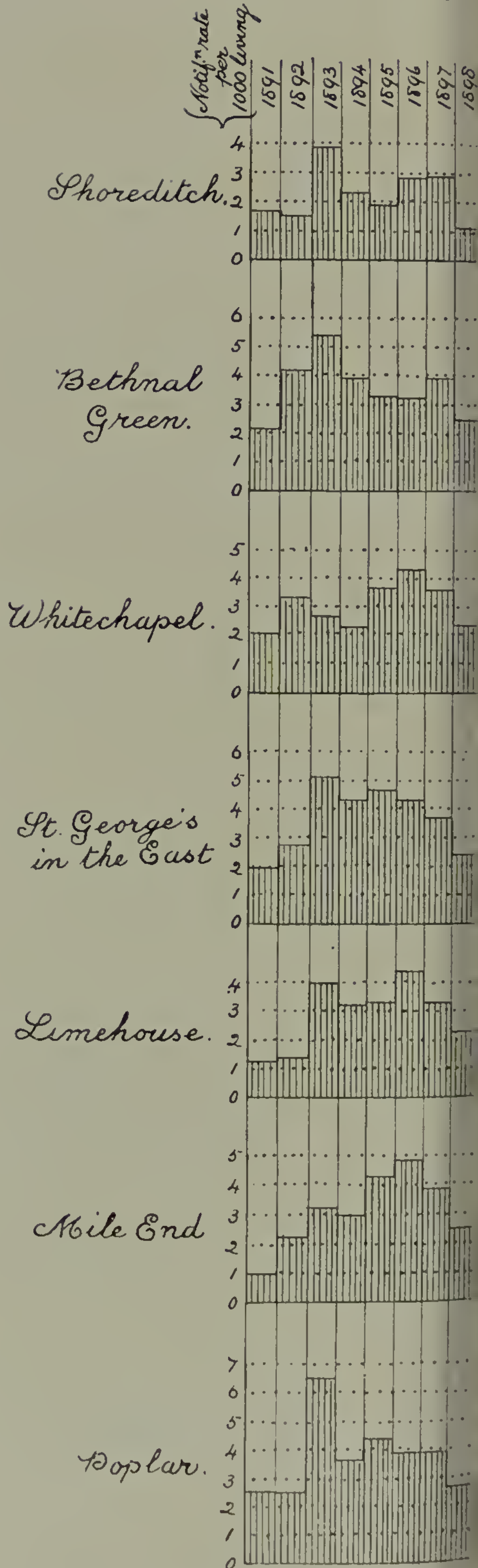
C

Central Districts



D

Eastern Districts



E

Southern Districts

It will, perhaps, be interesting for me here to bring under your notice the regulations of the School Board for London, and those of the Education Department, so far as they relate to infectious diseases in Schools.

After twelve months' experience of the work of the School Board in this connection, in 1891 the necessity for procuring accurate information to the School Board officials of the prevalence of infectious diseases in connection with Schools was forced upon my attention, and I was fortunate enough to induce the Government to cause the insertion of a clause in the Public Health (London) Act, October, 1891, to the following effect:

"Where a Medical Officer of Health receives a certificate under this section relating to a patient within the Metropolitan Asylums district, he shall within twelve hours after such receipt, send a copy thereof to the Metropolitan Asylums managers, and to the head teacher of the school attended by the patient (if a child) or by any child who is an inmate of the same house as the patient."

This clause, which represents for London a state of things in advance of the general health legislation for the rest of the country, is the foundation of the elaborate machinery which has been built up by the London School Board for successfully co-operating with the Metropolitan Sanitary Authorities in the prevention of infection, so far as this can successfully be done through the agency of the schools; and I should like to take this opportunity, if I may be permitted to do so, of emphasizing the fact that in my judgment the people of London are greatly indebted to the Metropolitan Medical Officers of Health for their great zeal and cordial co-operation with the School Board officials in this matter.

The following are extracts frcm the Code of Instructions to Teachers issued by the School Management Committee of the London School Board, and which were suggested by myself as their Medical Officer:

"The notification certificate of the Medical Officer of Health will be received by the head teacher, who must at once see that the communication is sent to the head teacher, or head

F

Specimen of page from Ledger for 1899 kept by School Boar

_____ School.

DISEASE.	Week.	JANUARY. 1st Week.—1st to 7th. 2nd ,, 8th ,, 14th. 3rd ,, 15th ,, 21st. 4th ,, 22nd ,, 28th. 5th ,, 29th ,, 31st. Infants.	Boys.	Girls.	Total for the Week.	FEBRUARY. 1st Week.—1st to 4th. 2nd ,, 5th ,, 11th. 3rd ,, 12th ,, 18th. 4th ,, 19th ,, 25th. 5th ,, 26th ,, 28th. Infants.	Boys.	Girls.	Total for the Week.	MARCH. 1st Week.—1st to 2nd ,, 5th ,, 3rd ,, 12th ,, 4th ,, 19th ,, 5th ,, 26th ,, Infants.	Boys.
Diphtheria.	1	1	1	—	2	—	—	—	—	—	—
	2	—	—	—	—	1	—	—	1	—	—
	3	—	—	—	—	—	—	—	—	—	—
	4	—	—	—	—	—	—	—	—	—	—
	5	1	—	—	1	—	—	—	—	—	—
Total ...		2	—	—	3	1	—	—	1	—	—
Scarlet Fever.	1	1	—	—	1	—	—	—	—	—	—
	2	1	—	—	2	1	—	—	1	—	—
	3	1	—	—	1	1	—	—	1	2	—
	4	—	—	—	—	1	—	—	1	1	—
	5	—	—	—	—	—	—	1	—	1	—
Total ...		3	—	—	4	3	—	1	5	4	—
Other Infectious Diseases.	1	1	—	—	2	—	—	—	—	—	—
	2	1	—	—	2	—	—	—	—	—	—
	3	—	—	—	—	—	—	—	—	—	—
	4	—	—	—	—	—	—	—	—	—	—
	5	—	—	—	—	—	—	—	—	—	—
Total ...		2	—	—	4	—	—	—	—	—	—

DISEASE.	Week.	JULY. 1st Week—2nd to 8th. 2nd ,, 9th ,, 15th. 3rd ,, 16th ,, 22nd. 4th ,, 23rd ,, 29th. 5th ,, 30th ,, 31st. Infants.	Boys.	Girls.	Total for the Week.	AUGUST. 1st Week.—1st to 5th. 2nd ,, 6th ,, 12th. 3rd ,, 13th ,, 19th. 4th ,, 20th ,, 26th. 5th ,, 27th ,, 31st. Infants.	Boys.	Girls.	Total for the Week.	SEPTEMBE 1st Week.—1st to 2nd ,, 3rd ,, 3rd ,, 10th ,, 4th ,, 17th ,, 5th ,, 24th ,, Infants.	Boys.
Diphtheria.	1	—	—	—	—	—	—	1	1	—	—
	2	—	—	—	—	—	—	—	—	—	—
	3	—	—	—	—	—	—	—	—	—	—
	4	—	—	—	—	—	—	—	—	—	—
	5	—	—	—	—	—	—	1	1	—	—
Total ...		—	—	—	—	—	—	2	2	—	—
Scarlet Fever.	1	1	—	—	1	2	—	—	2	—	—
	2	—	—	—	—	—	—	—	—	—	—
	3	2	—	—	2	1	—	—	1	—	1
	4	—	—	—	—	—	—	—	—	1	1
	5	—	—	—	—	—	—	—	—	1	—
Total ...		3	—	—	3	3	—	—	3	2	2
Other Infectious Diseases.	1	—	—	—	—	—	—	—	—	—	—
	2	—	—	—	—	—	—	—	—	—	—
	3	—	—	—	—	—	—	—	—	—	—
	4	—	—	—	—	—	—	—	—	—	—
	5	—	—	—	—	—	—	—	—	—	—
Total ...		—	—	—	—	—	—	—	—	—	—

...ulon for the Daily Registration of Infectious Disease Notifications.

__________ Division. __ Sanitary District.

...tal the ...ek.	APRIL. 1st Week.—1st. 2nd ,, 2nd to 8th. 3rd ,, 9th ,, 15th. 4th ,, 16th ,, 22nd. 5th ,, 23rd ,, 29th.			Total for the Week.	MAY 1st Week.—1st to 6th. 2nd ,, 7th ,, 13th. 3rd ,, 14th ,, 20th. 4th ,, 21st ,, 27th. 5th ,, 28th ,, 31st.			Total for the Week.	JUNE. 1st Week.—1st to 3rd. 2nd ,, 4th ,, 10th. 3rd ,, 11th ,, 17th. 4th ,, 18th ,, 24th. 5th ,, 25th ,, 30th.			Total for the Week.
	Infants.	Boys.	Girls.		Infants.	Boys.	Girls.		Infants.	Boys.	Girls.	
	—	—	—	—	—	—	—	—	—	—	—	—
	—	—	—	—	3	1	—	4	—	—	—	—
	—	—	—	—	—	—	—	—	—	1	—	1
	—	—	—	—	—	—	—	—	—	—	—	—
	—	—	—	—	—	—	—	—	—	—	—	—
	—	—	—		3	1	—	4	—	1	1	1
	—	—	—	—	1	—	—	1	—	—	—	—
	—	—	—	—	2	1	—	3	—	—	—	—
	—	—	—	—	2	—	—	2	1	—	—	1
	—	—	—	—	—	—	—	—	—	—	—	—
	1	—	—	1	1	—	—	1	1	—	—	1
	1	—	—	1	6	1	—	7	2	—	—	2
	—	—	—	—	—	—	—	—	—	—	—	—
	—	—	—	—	—	—	—	—	—	—	—	—
	—	—	—	—	—	—	—	—	—	—	—	—
	—	—	—	—	—	—	—	—	—	—	—	—
	—	—	—	—	—	—	—	—	—	—	—	—
	—	—	—	—	—	—	—	—	—	—	—	1

...al ...he ...k.	OCTOBER. 1st Week.—1st to 7th. 2nd ,, 8th ,, 14th. 3rd ,, 15th ,, 21st. 4th ,, 22nd ,, 28th. 5th ,, 29th ,, 31st.			Total for the Week.	NOVEMBER. 1st Week.—1st to 4th. 2nd ,, 5th ,, 11th. 3rd ,, 12th ,, 18th. 4th ,, 19th ,, 25th. 5th ,, 26th ,, 30th.			Total for the Week.	DECEMBER. 1st Week.—1st to 2nd. 2nd ,, 3rd ,, 9th. 3rd ,, 10th ,, 16th. 4th ,, 17th ,, 23rd. 5th ,, 24th ,, 31st.			Total for the Week.
	Infants.	Boys.	Girls.		Infants.	Boys.	Girls.		Infants.	Boys.	Girls.	
	—	—	—	—	—	—	—	—	—	—	—	—
	—	—	—	—	—	—	—	—	—	—	—	—
	—	—	—	—	—	—	—	—	—	—	—	—
	—	—	—	—	—	—	—	—	—	—	—	—
	—	—	—	—	—	—	—	—	—	—	—	—
	—	—	—	—	—	—	—	—	—	—	—	—
	—	—	—	—	—	1	1	2	—	—	—	—
	—	—	2	2	—	1	—	1	—	—	—	—
	1	1	1	3	—	—	—	—	—	—	—	—
	2	1	1	4	—	—	—	—	—	—	—	—
	—	—	—	—	—	—	—	—	—	—	—	—
	3	2	4	9	—	2	1	3	—	—	—	—
	—	—	—	—	—	—	—	—	—	—	—	—
	—	—	—	—	—	—	—	—	—	—	—	—
	—	—	—	—	—	—	—	—	—	—	—	—
	—	—	—	—	—	—	—	—	—	—	—	—
	—	—	—	—	—	—	—	—	—	—	—	—
		—	—	—	—	—	—		—	—	—	—

teachers, of the other department, or departments, of the school concerned, and each head teacher must initial and date the certificate.

"When the teacher has received this notification from the Medical Officer of Health, and taken all necessary action, he should note upon the certificate the action taken, endorse it with his name and the name of the school, and also state upon it whether the patient is a scholar of the school, and, if so, the department of the school which the patient attended before illness, and forward it immediately to the head office, addressed 'The Medical Officer, School Board for London, Victoria Embankment, W.C.' The teacher should likewise send notice of the case to the superintendent of visitors, if that has not already been done, on a form to be supplied for the purpose from the head office, care being taken to state the name of the child or family infected.

"Children excluded because of a notifiable infectious disease, or because of such an infectious disease in the houses in which they live, must not be allowed to return to school unless a certificate has been received from the Medical Officer of Health, stating that the premises are free from infection. Head teachers will note that the certificate forwarded by the Medical Officer of Health merely states that the premises from which the children come are free from infection, and does not certify that the children are in a condition to be permitted to resume attendance at school; for it may be that, though the premises are free from infection, the children coming from such premises may be sickening for an infectious disease. It will be necessary, therefore, for a further period of seven days to elapse before the return of such children to school, unless the Medical Officer of Health shall specially certify that a longer period of absence is necessary."

In the event of the head teacher not receiving the certificate stating that the premises are free from infection, it becomes his duty to send to the offices of the local authority in order that he may procure it.

The certificate, on its receipt by the Medical Officer, is at once entered to the credit of the school in what is practically an infectious ledger account in connection with each school of the Board, and which is kept in the manner shown on pp. 62, 63.

By this means the amount of infectious (notifiable) disease in connection with each school of the Board is under daily skilled supervision, and prompt action can be taken directly the necessity arises; for example, supposing the returns evidence an apparent prevalence or increase of disease, the head-teacher of the affected Department is requested to fill up and return immediately the accompanying form (Form II.).

FORM II.

School Board for London.

Outbreak of ______________ *at* ____________________ *School.*

Name.	Age.	Date of last Attendance at School.	Date of Notification.	Department.	Class-room.	Number on Roll in each Class-room.	Number in attendance in each Class-room.

Signature of Head Teacher ____________________

Date ______________

From this an analysis is made on Form III.

FORM III.

School Board for London.

RETURN OF CASES OF DIPHTHERIA.

______________ *Department.*

______________ *School.*

______ 1899.

Class-room.	Number on roll.	Number in Attendance.	Total No. of cases of Diphtheria	Last Attendance at School.		Period over which Outbreak extends.
				Cases.	Date.	
Totals ...						

Accommodation of Department ____________

And from a consideration of the sequence of the cases and the period of incubation, a judgment is formed as to the spread of the disease at the school. It may be, and frequently is, necessary that the school should at this time be visited by a skilled medical man for the purpose of examining into any condition which may suggest itself, including the examination of the children, and the Board are considering at this moment whether any further effective arrangements can be made in this respect. I know, of course, that it has been suggested that the Medical Officers of Health should have authority to enter Schools for the purpose of examining the children, but I question, apart from other reasons as to the wisdom of such an arrangement,

whether the School Board has legally the power to give this authority.

From a study of this evidence, it may be necessary to close a department or a class-room, in which case the committee concerned is so advised; or the disinfection of one or more rooms may be desirable, when the assistance of the Local Sanitary Authority is solicited. In any case a copy of the return and all the facts of the case are brought under the notice of the Medical Officer of Health interested, and a conference by telephone or otherwise obtained.

Further, if any children in attendance at school show symptoms of an infectious disease, they are at once to be excluded, and intimation given both to the Medical Officer of Health and to the medical officer of the Board; and for this purpose the teachers are instructed in the various symptoms of the different infectious diseases.

The action of the School Board as regards such Sunday-schools as they can control is none the less satisfactory.

It is one of the conditions of letting a Board School to the managers of a Sunday-school that the following regulations should be observed:

(*a*) When the Medical Officer reports that infectious disease is prevalent in any school, the Board may direct the Divisional Superintendent to prepare a list of the houses, children in which are excluded from school either on account of personal illness or illness in the house.

(*b*) That a copy of this list be forwarded every Thursday to the Sunday-school tenant, and that he be required to exclude the children from these houses until the houses have been disinfected by the proper sanitary authority.

(*c*) That a list of such houses as have been disinfected shall be forwarded by the Superintendent each week to the Sunday-school tenant.

The action of the Education Department in this connection is governed by Articles 88 and 101 of the Education Code as follows:

88. The managers must at once comply with any notice of the Sanitary Authority of the district in which the school is situated, or any two members thereof acting on the advice of the Medical Officer of Health, requiring them for a specified time, with a view

to preventing the spread of the disease, or any danger to health likely to arise from the condition of the school, either to close the school or to exclude any scholars from attendance, but after complying, they may appeal to the Department if they consider the notice to be unreasonable.

101. Where the Department are satisfied that by reason of a notice of the Sanitary Authority under Article 88 or any provision of an Act of Parliament requiring the exclusion of certain children, or by reason of the exclusion under medical advice of children from infected houses, the average attendance has been seriously diminished, and that consequently a loss of annual grant would, but for this Article, be incurred, the Department have power to make a special grant not exceeding the amount of such loss, in addition to the ordinary grant.

Table X. is interesting as evidencing the action which, in view of the prevalence of diphtheria, the Medical Officers of Health of the Metropolis, of whom there are fifty-one, have thought it necessary to take in connection with school closure during the past four years. I think it is a fair deduction to make that these gentlemen are not convinced schools have exerted a very great influence in the matter.

TABLE X.

Showing the closure of schools or class-rooms of London School Boards for Diphtheria for the years 1896 *to* 1899.

Year.	Number of Children on Board School Roll.	Name of School, with Accommodation.	Class-rooms closed, with Accommodation.		
			Boys.	Girls.	Infants.
1896	511,566	None	—	—	—
1897	520,877	Harwood Road (1,188)	—	73	—
1898	527,486	Tottenham Road (1,448)	—	—	65
		St. Dunstan's Road (1,586)	—	—	148
		William Street (1,368)	—	—	74
		Ackmar Road (1,590)	—	—	78
		Haverstock Hill (1,187)	—	740	447
1899	533,855	Plough Road (1,363)	—	—	523
		Ackmar Road (1,590)	—	—	630
		Star Lane (1,202)	—	—	82
		Heber Road (1,602)	—	—	642

Five of these schools were in the same sanitary area.

With regard to the precautions which are taken in the provincial towns and abroad to check the spread of diphtheria by schools, there is little to be said. The steps taken are very similar to those adopted in London, and indeed in most cases these have been taken as the guide. They consist chiefly of notification, removal of the affected scholar, keeping away from school the other members of the family, and occasionally disinfection of the class-room, or closure of school.

The precautions taken at Providence, U.S.A., are more elaborate, and are worth quoting in this connection. Dr. Chaplin writes:

"When a case is reported, a placard is placed on the house stating that there is a case within, and for purposes of isolation croup is treated as diphtheria. A notice is sent to the school and Sunday-school excluding all children in the family and all children in the house if it is a crowded tenement. If it is desired to send a child away from home, it is required that a culture shall first be taken from the throat to show whether diphtheria bacilli are present. If not, the child may leave the house, and continue in school. After the disease is over, a *negative culture is required from every member of the family before the children are allowed in school*. . . . If a school epidemic again occurred, I should take cultures from everyone in school, perhaps on two or three successive days, and exclude all who showed diphtheria bacilli."

It is well worth while considering whether some such sort of examination might not be adopted with advantage in London.

LECTURE III.

Diphtheria, then, is a disease occasioned by the presence of a particular bacillus, which for all practical purposes is found alone in the affected area and its neighbourhood, and which in the course of growth and multiplication forms a toxin, or poison; and this poison, subsequently becoming absorbed into the system, gives rise to the general symptoms with which we are all familiar. I have said that for all practical purposes this is the case, but it must be noted that diphtheria bacilli have been found in the glands and in the spleen, and probably in other organs.

These toxic products are therefore of the greatest importance. Roux and Yersin were the first to show that by the injection of the toxic products of the diphtheria bacilli into susceptible animals the nervous lesions characteristic of the disease could be artificially induced, and these observations were confirmed by Brieger, Fränkel, and Sidney Martin.

Toxins vary greatly in their composition, and consequently differ in what may be called their lethal activity, and in their local or swelling-producing activity, one specimen containing a considerable proportion of the substance which determines the local effect, but a smaller amount of the substance causing the death of the animal; whilst a second toxin may set up only a slight local reaction but cause death in a comparatively short space of time. In diphtheria it is the lethal action of the poison which has to be reckoned with, and in the successful treatment of the disease,

therefore, the activity of antitoxic serum is determined by ascertaining its power of neutralizing this lethal activity as accurately as possible. The lethal factor is the one of importance, and Ehrlich, to whose researches we are so greatly indebted, emphasizes this when he advises that the time of death of an inoculated animal should be taken as the determining factor in judging of the activity of a test toxin, and consequently of the neutralizing or antidotal power of an antitoxin.

In order to determine the absolute toxicity of a toxin Ehrlich took the death period as four days from the day of infection, so that if the animal lived beyond the fourth day, the dose of toxin would be considered sub-lethal. He pointed out that, owing to the varying susceptibility of the animals, the dose might kill some of them in two days, while a certain number of them might live to the fourth day, but if the dose were strong enough, no animal should live beyond that day. Theoretically 100 times this dose, injected along with one unit of antitoxin, should not kill before the fourth day, on which day the animal might die, but it certainly should not live beyond the fifth or sixth day. It was found, however, that this multiple of 100 plus the unit of antitoxin did not give these definite results. He then determined accurately two neutralization points—first the amount of toxin which one antitoxin unit exactly neutralizes—*i.e.*, the effect on the animal after injection would be such that not only would the animal not die, but that no ill-effects would follow. This point he represented at L_0, nothing being left to be neutralized. The second neutralization point was that at which the quantity of toxin present is not only sufficient to neutralize the whole of the antitoxin, but a sufficient quantity of uncombined toxin remains sufficient to kill the animal on the fourth day—this point he represents as L_x. Theoretically the difference between the two L_0 and L_x should be 100 and 101 multiples of the single dose respectively. In the first case there is complete neutralization, in the second an excess of toxin sufficient to kill the animal in the same time that a single lethal dose would bring about the same result. This method, however, is not in actual practice.

Ehrlich further shows that there is a definite chemical action

and reaction between toxin and antitoxin, neutralization going on more quickly in concentrated solutions than in diluted ones. Heat accelerates and cold retards the combination, and these, it will be noted, are precisely the conditions under which ordinary chemical double salts are formed. He thus was led to look upon the neutralization of toxins by antitoxins as the formation of a double salt; and arguing from this analogy, he laid down the rule that one equivalent of the toxin always neutralizes an equivalent of the anti-substances, and that multiples of the one neutralize corresponding multiples of the other. A molecule of the toxin binds, therefore, a definite and constant quantity of the anti-substances, for which also it has a specific affinity.

A further suggestion by Ehrlich, which is of supreme interest in this connection, is that small quantities of the tetanus toxin are actually selected by the motor ganglion cells of the central nervous system from the fluids in which the toxin is conveyed throughout the body, and firmly held by such cells. Every functional cell consists primarily of a nucleus, associated with which is the main function of the vitality of the cell. In addition there are associated "lateral chains" with subsidiary or special functions. These chains have specific combining functions, one chain especially having a special affinity for the tetanus poison which is literally seized upon by the living protoplasm of the cell, and by this means, the lateral chain is subjected to the continued influence of the attached tetanus poison, which—to use Ehrlich's words—"brings about a slowly-advancing but long-continuing functional disturbance so long as the union of the lateral chain and toxin continues," and this union generally remaining permanent, there is an explanation of the formation of the anti-substances.

This function of the lateral chains to hold the toxin is something apart from the ordinary cell activity. As fresh toxin is presented, so there is induced in the cell a greater and greater power of combining with the toxin, this power assuming a particulate character according as the toxin molecule be that of diphtheria, tetanus, snake-poison, or the like, and as fresh supplies of toxin are provided, new lateral chains are formed, having the

specific power of combining with the specific toxin. These chains become developed to such an extent that they can no longer be retained in the cell, but are thrown off into the blood unused, ready to come into contact with the specific molecules for which they have affinity—indeed, under such circumstances they appear to have a greater power of combination than they possessed when present in the cell.

Another interesting point is that even large doses of the toxins, with the exception of the snake-poison, require a considerable time in which to exert their toxic effects. Ehrlich suggests that this is because the toxin is forming a definite molecular combination with the protoplasm of the cell or its lateral chain, and that having entered into the combination, it does one of two things: either it paralyzes the cell, thus interfering with its main functions; or it so stimulates its special function that, in place of succumbing, it gradually acquires the power of combining with and rendering harmless larger and larger doses of toxin. In the one case, the death of the cells and the animal occurs; in the other the formation of antitoxin.

Further, Ehrlich asserts that if the special cells of an animal or organ do not possess lateral chains that can unite with the toxin molecule, the toxin does not prove fatal to these cells, and no antitoxin is produced. The obvious bearing of this upon the production of antitoxin by susceptible animals, and the failure of all attempts to reproduce it in animals immune to certain of these organic poisons, is of great interest.

Roux and Yersin obtained the toxin of diphtheria by precipitation with alcohol and phosphate of lime, and therefore they looked upon it as a ferment or an enzyme, Brieger and Fränkel saw in it a tox-albumin or a mixture of such, whilst Professor Sidney Martin, in a report to the Local Government Board (on "The Chemical Pathology of Diphtheria and of Infective Endocarditis; with an Account of Diphtheria Palsy, experimentally produced by the Chemical Poison of Diphtheria"), describes how he obtained an albumose and an organic acid from the blood and organs of patients who had died of diphtheria. The albumose was indistinguishable in its chemical reactions from the deutero-

albumose of peptic digestion; but its physiological action was entirely different. Injected under the skin of animals, a single dose produced a local œdema, which disappeared in the course of thirty-six hours, together with an occasional slight rise of temperature. Small multiple doses in rabbits produced fever, lasting for some days, paresis of the hind limbs and loss of weight, followed by loss of power in the fore limbs, and finally by death. An examination of the nerves showed that in many of them the white substance of Schwann had been broken up, and that degeneration of the nerve fibre below this level had taken place.

This albumose is capable of remaining in the blood for a considerable period after a single injection. In one case Martin found evidence of its presence ten days after the injection.

The organic acid, which is a yellow, amorphous body, is capable of producing the same effects as the albumose, but is apparently less toxic.

Similar poisons still more active were obtained from the diphtheritic membranes, and Professor Sidney Martin was also able to separate an albumose from artificial cultures of the diphtheria bacillus having similar properties.

Professor Sidney Martin considers that the bacillus of diphtheria is further capable of producing an enzyme at the site of the local lesion, corresponding to the toxin of Roux and Yersin, and that this enzyme is able to manufacture an albumose and an organic acid from the albuminous substances in the human tissues, especially the spleen.

Dr. Cartwright Wood confirmed Sidney Martin's experiments by obtaining from cultures an albumose having a similar action on horses to those described by him.

If such a toxin be kept in a warm chamber, it begins to lose its toxic effects, while its power to neutralize an antitoxin remains unimpaired. This is an important fact to remember in keeping a test toxin for standardizing an antitoxin.

Further, Dr. Cartwright Wood, who had previously pointed out that, in order to artificially obtain the toxins of the microbe as formed in the human subject, it was necessary to give it albumin in its culture medium, so as to place it as nearly as possible under

analogous conditions to that which pertained in man, obtained an active growth of the bacillus by inoculating broth with a virulent culture, and after the lapse of a day or two added 10 to 20 per cent. of horse serum, or plasma, in order that the enzyme or ferment toxin produced from the broth might not alone be formed, but also the albumoses from the dilute albumin. The culture was then kept in an incubator for three or four weeks, and again inoculated on fresh medium, the best growth appearing to result when this procedure was repeated three or four times, and the growth allowed to continue for three to six months; afterwards the culture was subjected to a temperature of 65° C. for about an hour. By this latter process the ferment toxin is destroyed, and on filtering off the bodies of the bacilli, a fluid remains containing but little lethal activity, and incapable of causing much local irritation, but capable of setting up marked febrile reaction; and Dr. Cartwright Wood adds that, as the diphtheria albumose described by Sidney Martin had these properties, the potency of the serum toxin depended on the presence of this body. By this means the lethal activity of the toxin is lost, while its property of rendering animals more or less immune is retained, just as Ehrlich had previously shown that similar properties were present in the case of tetanus toxin after the addition of certain quantities of bisulphide of carbon. This fact at once suggested the possibility that its application would shorten the preliminary treatment which a horse had to undergo before it could receive the large doses of the broth or ferment toxin necessary for the production of an antitoxin of any strength, and on applying this method, it was found that not only was immunity produced, but a considerable quantity of antitoxin was formed, for whilst a horse which received 2180 c.c. of serum toxin in the course of a fortnight yielded a serum containing 50 units per c.c., if it were injected with a mixture of serum toxin and a small quantity of comparatively weak ordinary toxin, its serum rose in antitoxic value to 125 units per c.c. It was further found by Professor Sims Woodhead and Dr. Cartwright Wood that the best results were obtained when a kind of cumulative action was just maintained, by which means the animal was kept in a chronic

condition of reaction, the most potent antitoxin being thus more rapidly obtained than in any other way.

The conclusions which Dr. Cartwright Wood arrived at as the result of this interesting series of experiments with albumoses may be given at length, so important are they in connection with the treatment of diphtheria. They are: "(1) That powerful diphtheria antitoxins can be produced without risk in a much shorter period of time than has been previously possible; (2) that much more powerful antitoxins can be easily produced, so that the amount necessary to be injected into a patient can be greatly reduced, and one of the main objections to its introduction into private practice in this country removed; (3) that the greater strength of the serum will permit of the patient receiving at the beginning a sufficient quantity of the serum at one injection, when, as is universally recognised both by animal experiment and clinical experience, its curative action is exerted most markedly."

Ehrlich has shown that when toxin is kept in a warm chamber, or even at the ordinary temperature for a time, it loses its toxic activity, but still retains its power of combining with diphtheria antitoxin. These modified toxins, which still retained the specfic power of combination, he calls "toxoids," and he shows that different crude diphtheria toxins have differing lethal activities, and combining powers from those produced by the transformation of lethal toxins into comparatively non-lethal toxoids. These toxoids may be conveniently divided into toxoids and epitoxoids, the toxoids representing everything in the mixture which is not toxin or epitoxoid, but which has the power of neutralizing certain proportions of antitoxin. The epitoxoids appear to have a combining power less than that possessed by toxin; and it is remarkable that the epitoxoids, although negative in their action in other directions, appear to exercise a certain trophic action on the nerves, especially when introduced in large quantities.

Ehrlich came to the conclusion that at some period or other all toxins have theoretically an exact lethal dose corresponding with ts power of combining with antitoxin, by which it is exactly neutralized, and assuming that this lethal dose is found, a hundred

times this amount should exactly neutralize one antitoxin unit; as time goes on, if the broth culture be kept in an incubator or warm room, or exposed to light, epitoxoids are formed, while other toxoids appear if the temperature be low.

In considering questions relating to this subject it is as well that we should have a standard in our minds of the strength of the toxin we propose to talk about, and for this purpose we shall find it convenient to adopt that of Behring, which is that in every c.c. of standard toxin there is sufficient lethal substance present to prove fatal in four days to 100 guinea-pigs, each weighing 250 grammes. This he calls normal toxin, and expresses it as DTN^1. If there were only 10 lethal doses in a c.c. it would be written $DTN^{0\cdot1}$, and if 140, DTN1·4.

But, owing to the difficulty of obtaining a standard toxin, it is now usual to take a standard antitoxin, or, in other words, to make our calculations in terms of antitoxin rather than in terms of toxin, bearing in mind the theoretical standard of Behring; for this purpose antitoxin is taken of a strength of 18 units, or, in other words, antitoxin, which is $\frac{1}{18}$ of this strength, would be equal to a unit, which in its turn would be equal to 100 nominal lethal doses of antitoxin.

We may know the lethal dose of toxin for a guinea-pig, but we do not know the lethal dose for a human being, and consequently it is wise in the treatment of diphtheria to inject a large dose of antitoxin, say 4,000 units, which would have an equivalent of 400,000 lethal doses of toxin for a guinea-pig.

After these preliminary remarks let us now consider the steps necessary for the preparation of antitoxic serum. The toxin is prepared by the growth of the diphtheria bacillus in nutrient bouillon, prepared by taking a pound of veal, from which all fat and connective tissue has been removed, mincing it, and adding to it 800 c.c. of water, allowing it to stand for two or three hours, and then boiling it for twelve hours, care being taken to keep the meat from running together in masses by shaking it; the fluid is then expressed from the meat in a press, and 2 per cent. of Witte's peptone added; it is afterwards boiled for an hour, allowed to cool, and filtered; it is then heated

to the boiling-point, and neutralized or rendered faintly alkaline to phenol phthalein with normal sodium hydrate solution, about 30 to 33 c.c. of normal sodium hydrate solution being required per litre; after neutralization it is again boiled for two hours, filtered, and transferred to the flasks in which the toxin is to be produced, and which resemble a Wolfe's bottle, having three necks; this shape of flask is taken so as to ensure a good surface growth. 400 c.c. of broth are placed in each flask.

The broth is inoculated with an organism, which has been specially chosen for its virulence, and the flask is kept at a temperature of 35° C., or from 30° to 36·5°, some bacilli producing a more active toxin at the lower, others at the higher, or at an intermediate, limit. In the course of twenty-four hours a diffuse cloudiness takes place in the liquid, due to the formation of dust-like granules or small flakes, which sink to the bottom as a flocculent sediment. The turbidity and sediment increase in proportion to the activity and vigour of the organism; at the same time a film is formed on the surface which is easily broken up by shaking, when it sinks to the bottom; the opalescence remains as long as the alkalinity of the medium is maintained and growth continues; when this has ceased, the flocculi sink to the bottom, the broth resumes its original clearness, and the formation of toxin ceases, although the bacilli are alive in the sediment; this film-formation is important as an indication of strong toxin production.

If the reaction of an inoculated alkaline broth be tested at intervals, an acid reaction will be noted which increases during the first two or three days after inoculation; then comes a pause, and finally the broth appears to regain its alkalinity; if the broth be acid or but faintly alkaline, no good toxin is produced.

The growth of the pseudo-diphtheria bacillus is also vigorous in broth, but the cloudiness is more dense, sets in earlier, and the broth becomes clear much later; there is also an absence of acid production in the early days of growth.

The toxin is then poured into properly sterilized jars, where the bacilli rapidly settle in a thick deposit. The supernatant liquid is at once filtered through a Chamberland filter, and the strength of the toxin as regards its lethal activity tested, and the result recorded on the flask which contains it.

I have already insisted upon the fact that there are two toxins, a ferment toxin to be obtained from broth in the way just described, and an albumose toxin obtained from the growth of the organism in serum, and that by the use of this latter an animal may be rendered immune more rapidly, and so be placed sooner in a condition to supply antitoxin. This serum toxin is prepared by making a bouillon cultivation of the diphtheria bacillus in the ordinary way in a flask holding 1 or 2 litres. After an interval of twenty-four hours, if the growth be sufficiently vigorous, 300 c.c. of horse serum, kept absolutely sterile, are added by means of a large sterile pipette, and the flask replaced in the incubator. In place of serum, citrate plasma may be used, but in this case all the lime must be removed by the addition of oxalate of soda and subsequent filtration. The bottle is shaken daily for several days, a vigorous growth takes place, and a considerable deposit is formed. From time to time a fresh quantity of serum and a fresh vigorous culture of diphtheria is added. This growth is allowed to remain in the incubator for one or two months, and in this case the active lethal toxicity of the broth need not be maintained. When the deposit is about half an inch or more in thickness, the fluid is placed in a thin flask, and immersed in water having a temperature of 65° to 68°. As soon as a thermometer placed through the neck of the flask into the middle of the fluid registers 60° to 65°, the time necessary for the exposure of the fluid to the temperature has commenced, and it must be continued for one hour. By this means the diphtheria bacilli are killed, and the ferment toxin destroyed. The heated fluid is then allowed to remain until the dead bacilli fall to the bottom, after which the clear supernatant fluid is decanted and filtered several times with proper precautions through a small Chamberland filter.

The Antitoxin is obtained by taking a horse, and testing it for glanders and tubercle in the first instance by the use of mallein and tuberculin so as to be assured that the animal is free from these diseases. An injection is then made subcutaneously in the neck of 300 c.c. of the serum toxin; this, according to the amount of reaction obtained, is followed by a similar injection of 400 c.c. in two or three days, and so on persistently for about four weeks.

In this way the animal is rendered immune, and then injections of the ordinary ferment toxin may be commenced, 400 c.c. being first used, and repeated every three or four days, the doses being gradually increased until 500 or 600 c.c. are injected. The blood is carefully tested from time to time throughout the treatment, and in this way it can be determined when the blood is ready to be drawn. The blood is eventually drawn by making a small incision through the skin over the jugular vein—slight pressure being exerted on the vein below the point of intended orifice—and then by introducing a trocar and canula, to which latter is attached a piece of indiarubber tubing, and which is arranged to discharge its contents into a sterile beaker of a capacity of 800 c.c., covered with parchment paper, and containing 6 or 7 c.c. of a 10 per cent. solution of citrate of soda. The addition of this salt delays the clotting of the blood, so that the red cells have time to fall to the bottom, by which means an exaggerated buffy clot is formed. At the end of twenty-four or forty-eight hours nearly one-half of the bulk of the blood is drawn off as serum, and if the clot be allowed to stand a day or two longer another 5 or 10 per cent. more may be obtained. The serum is drawn off by a system of exhaustion into a sterilized conical flask, graduated in half-litres, and to each litre is added 30 c.c. of a 6 per cent. emulsion of trikresol, so as to make the serum an impossible medium for organisms to grow in. The serum in bulk is then transferred to a cool, dark room. No other special precautions being called for, it is then tested and brought up to a proper standard with other antitoxins of known strength, and ultimately sent out in small tubes containing 4,000 units in 10 c.c. for a dose.

The use of antitoxic serum for the treatment of diphtheria cases has now for some time been general in the hospitals of the Metropolitan Asylums Board; let us therefore look for the results to the statistical evidence available from these institutions.

Table I. shows the mortality per cent. of the Diphtheria cases admitted into all the Board's Hospitals for each year since 1889 —the first complete year after Diphtheria was recognised as a disease admissible to the Board's hospitals.

TABLE I.

Mortality per cent. of Diphtheria cases admitted during the years 1889 to 1898 into the Hospitals of the Metropolitan Asylums Board.

Hospital.	1889.	1890.	1891.	1892.	1893.	1894.	1895.	1896.	1897.	1898.
Eastern -	44·21	38·49	33·22	35·67	35·24	30·29	25·94	17·37	17·18	15·91
N.-Western	31·60	31·42	22·10	21·83	26·48	27·10	24·55	29·75	18·81	19·87
Western -	35·82	21·87	38·43	32·09	38·13	34·03	19·95	21·93	17·50	16·33
S.-Western -	—	—	23·84	22·50	27·18	26·48	22·17	16·39	17·60	11·96
Fountain -	—	—	—	—	—	39·04	19·47	19·72	20·86	14·41
S.-Eastern -	37·11	32·00	47·50	56·60	39·91	27·60	22·78	20·26	17·06	16·55
Park - -	—	—	—	—	—	—	—	—	17·39	13·23
Brook -	—	—	—	—	—	—	—	21·47	13·11	12·43
Northern -	—	—	0·41	0·47	—	—	0·719	0·30	0·134	0·12
Total -	40·74	33·55	30·61	29·51	30·42	29·29	22·85	21·20	17·69	15·37

The total mortality rates are therefore as follows:

1889	40·7	1894	29·2
1890	33·5	1895 (first antitoxin year)	22·8
1891	30·6	1896	21·2
1892	29·5	1897	17·7
1893	30·4	1898	15·4

by which it will be seen that in 1898 the mortality had been reduced by the use of antitoxin by nearly 50 per cent.

Tables II. and III. show the admissions, deaths, and mortality per cent. of diphtheria cases at each of the hospitals of the Board during the years 1890, 1891, 1892, 1893, and 1898 respectively. Four years are selected as the pre-antitoxin period, in order to obtain a number of cases as nearly as possible equal to the number treated in 1898, which is the latest year of the antitoxin period for which figures are obtainable.

All cases of diphtheria are included in the tables, including those who died within forty eight hours of admission, and those who died from intercurrent maladies.

Table II.

Gives the admissions, deaths, and discharges of Diphtheria cases admitted into the Hospitals of the Metropolitan Asylums Board during the years 1890 *to* 1893.

Hospital.	Remaining at beginning of year.	Admitted.		Total treated.	Discharged.		Died.	Mortality per cent.	Remaining at end of year.
		Direct from homes.	From other hospitals.		Re-covered.	To other hospitals.			
1890—									
Eastern	56	393	—	449	111	138	153	38·49	47
North-Eastern	—	—	—	—	—	—	—	—	—
North-Western	23	265	—	288	170	5	83	31·42	30
Western	8	130	—	138	19	79	28	21·87	12
South-Western	—	14	—	14	—	—	4	—	10
Fountain	—	—	—	—	—	—	—	—	—
South-Eastern	14	140	—	154	69	25	48	32·00	12
Northern	30	—	247	277	257	—	—	—	20
Gore Farm	—	—	—	—	—	—	—	—	—
Total	131	942	247	1,073	626	247	316	33·55	131
1891—									
Eastern	47	465	—	512	125	186	155	33·22	44
North-Eastern	—	—	—	—	—	—	—	—	—
North-Western	30	386	—	416	306	—	86	22·10	24
Western	12	141	—	153	31	55	54	38·43	13
South-Western	10	201	—	211	124	—	44	23·84	43
Fountain	—	—	—	—	—	—	—	—	—
South-Eastern	12	119	—	131	60	4	57	47·50	10
Northern	20	—	245	265	237	—	1	0·41	27
Gore Farm	—	—	—	—	—	—	—	—	—
Total	131	1,312	245	1,443	883	245	397	30·61	161
1892—									
Eastern	44	556	—	600	208	148	198	35·67	46
North-Eastern	—	—	—	—	—	—	—	—	—
North-Western	24	648	10	682	468	—	138	21·83	76
Western	13	247	—	260	105	56	78	32·09	21
South-Western	43	420	—	463	303	10	93	22·50	57
Fountain	—	—	—	—	—	—	—	—	—
South-Eastern	10	138	—	148	52	—	75	56·60	21
Northern	27	—	204	231	222	—	1	0·47	8
Gore Farm	—	—	—	—	—	—	—	—	—
Total	161	2,009	214	2,170	1,358	214	583	29·51	229
1893—									
Eastern	46	510	—	556	279	57	181	35·24	39
North-Eastern	—	7	—	7	2	1	2	33·33	2
North-Western	76	1,249	—	1,325	900	26	332	26·48	67
Western	21	256	—	277	136	7	94	38·13	40
South-Western	57	585	—	642	432	—	160	27·18	50
Fountain	—	—	—	—	—	—	—	—	—
South-Eastern	21	241	—	262	143	1	96	39·91	22
Northern	8	—	74	82	82	—	—	—	—
Gore Farm	—	—	—	—	—	—	—	—	—
Total	229	2,848	74	3,077	1,974	92	865	30·42	220
Grand totals	652	7,111	780	7,763	4,841	798	2,161	30·62	741

Table III.

Gives the admissions, deaths, and discharges of Diphtheria cases admitted into the Hospitals of the Metropolitan Asylums Board in 1898.

Hospital.	Remaining at beginning of year.	Admitted.		Total treated.	Discharged.		Died.	Mortality per cent.	Remaining at end of year.
		Direct from homes.	From other hospitals.		Re-covered.	To other hos-pitals.			
1898—									
Eastern - -	184	1,274	1	1,459	817	279	205	15·91	158
North-Eastern	—	8	—	8	7	—	—	—	1
North-Western	86	890	—	976	705	—	176	19·87	95
Western - -	92	786	—	878	367	252	125	16·33	134
South-Western	94	577	—	671	432	91	70	11·96	78
Fountain -	92	732	—	824	453	180	106	14·41	85
South-Eastern	115	734	1	850	542	42	119	16·55	147
Park - -	38	810	—	848	561	6	96	13·03	185
Brook - -	119	755	—	874	648	—	93	12·43	133
Northern -	75	—	848	923	803	—	1	0·12	119
Gore Farm -	—	—	—	—	—	—	—	—	—
Total - -	895	6,566	850	7,461	5,335	850	991	15·37	1,135

If we compare Table II. with Table III. it will be seen that the latter shows a remarkable lowering of the combined general mortality, namely, from 30·62 to 15·37.

At every hospital the rate of mortality fell, the lowest being at the South-Western Hospital, where it dropped from 22·50 in 1892 to 11·96 in 1898.

Tables IV. and V. give the admissions and deaths, divided according to age and sex, and the mortality per cent. of these cases.

Table IV.

Admissions and deaths of Diphtheria cases admitted into the Hospitals of the Metropolitan Asylums Board, divided according to age and sex, for the years 1890 *to* 1893.

Ages.	1890.						1891.					
	Males.		Females.		Total.		Males.		Females.		Total.	
	Admissions	Died.	Admissions.	Died.			Admissions.	Died.	Admissions.	Died.		
Under 1 -	6	4	5	3	11	7	13	12	13	8	26	20
1 to 2 - -	26	17	27	22	53	39	41	23	32	19	73	42
2 ,, 3 - -	37	26	44	34	81	60	45	29	61	35	106	64
3 ,, 4 - -	62	27	42	15	94	42	60	29	85	38	145	67
4 ,, 5 - -	49	27	51	23	100	50	55	26	78	38	133	64
Total under 5	170	101	169	97	339	198	214	119	269	138	483	257
5 to 10 - -	136	46	149	49	285	95	188	47	216	67	404	114
10 ,, 15 - -	47	2	72	13	119	15	62	4	101	12	163	16
15 ,, 20 - -	19	—	52	1	71	1	28	2	54	—	82	2
20 ,, 25 - -	19	1	31	2	50	3	31	1	42	3	73	4
25 ,, 30 - -	12	—	24	—	36	—	9	—	37	—	46	—
30 ,, 35 - -	12	—	11		23	—	15	1	9	1	24	2
35 ,, 40 - -	4	1	6	—	10	1	3	—	10	—	13	—
40 ,, 45 - -	—	—	3	1	3	1	6	—	6	—	12	—
45 ,, 50 - -	2	—	1	1	3	1	4	—	3	2	7	2
50 ,, 55 - -	—	—	—	—	—	—	—	—	2	—	2	—
55 ,, 60 - -	—	1	2	—	2	1	1	—	2	—	3	—
And upwards	1	—	—	—	1	—	—	—	—	—	—	—
Total - -	422	152	520	164	942	316	561	174	751	223	1,312	397

Table IV. (*continued*).

Ages.	1892.						1893.					
	Males.		Females.		Total.		Males.		Females.		Total.	
	Admissions.	Died.	Admissions.	Died.			Admissions.	Died.	Admissions.	Died.		
Under 1 - -	28	14	21	17	49	31	18	15	22	12	40	27
1 to 2 - -	54	40	54	26	108	66	88	55	78	55	166	110
2 ,, 3 - -	77	45	86	45	163	90	117	73	102	49	219	122
3 ,, 4 - -	94	48	101	48	195	96	158	90	138	65	296	155
4 ,, 5 - -	101	39	139	67	240	106	154	61	185	64	339	125
Total under 5	354	186	401	203	755	389	535	294	525	245	1,060	539
5 to 10 - -	301	74	330	89	631	163	403	114	477	139	880	253
10 ,, 15 - -	84	8	125	7	209	15	135	18	163	17	298	35
15 ,, 20 - -	62	2	99	2	161	4	92	6	125	5	217	11
20 ,, 25 - -	45	1	74	2	119	3	44	1	100	4	144	5
25 ,, 30 - -	19	2	42	2	61	4	48	4	65	5	113	9
30 ,, 35 - -	12	—	21	1	33	1	18	1	34	2	52	3
35 ,, 40 - -	5	1	10	1	15	2	19	1	23	—	42	1
40 ,, 45 - -	4	—	9	—	13	—	9	2	8	2	17	4
45 ,, 50 - -	2	—	3	—	5	—	2	—	9	1	11	1
50 ,, 55 - -	1	—	3	1	4	1	5	2	1	—	6	2
55 ,, 60 - -	—	—	1	—	1	—	3	1	2	—	5	1
And upwards	—	—	2	1	2	1	1	—	2	1	3	1
Total - -	889	274	1,120	309	2,009	583	1,314	444	1,534	421	2,848	865

TABLE IV. (*continued*).
Summary 1890 *to* 1893.

Ages.	Males.			Females.			Total Admissions.	Total Died.	Combined Mortality per cent.
	Admissions.	Died.	Mortality per cent.	Admissions.	Died.	Mortality per cent.			
Under 1 - -	65	45	69·23	61	40	65·57	126	85	67·46
1 to 2 - -	209	135	64·59	191	122	63·87	400	257	64·25
2 ,, 3 - -	276	173	62·68	293	163	55·63	569	336	59·05
3 ,, 4 - -	364	194	53·30	366	166	45·35	730	360	49·31
4 ,, 5 - -	359	153	42·62	453	192	42·38	812	345	42·49
Total under 5	1,273	700	54·99	1,364	683	50·07	2,637	1,383	52·44
5 to 10 -	1,028	281	27·33	1,172	344	29·35	2,200	625	28·41
10 ,, 15 -	328	32	9·76	461	49	10·63	789	81	10·27
15 ,, 20 -	191	10	5·23	330	8	2·42	531	18	3·39
20 ,, 25 -	139	4	2·88	247	11	4·45	386	15	3·89
25 ,, 30 -	88	6	6·82	168	7	4·17	256	13	5·07
30 ,, 35 -	57	2	3·51	75	4	5·33	132	6	4·54
35 ,, 40 -	31	3		49	1		80	4	
40 ,, 45 -	19	2		26	3		45	5	
45 ,, 50 -	10	—	12·5	16	4	10·18	26	4	11·11
50 ,, 55 -	6	2		6	1		12	3	
55 ,, 60 -	4	2		7	—		11	2	
And upwards	2	—		4	2		6	2	
Total - -	3,176	1,044	32·87	3,925	1,115	28·41	7,111	2,161	30·39

TABLE V.

Admissions and deaths of Diphtheria patients into the Hospitals of the Metropolitan Asylums Board during 1898, *divided according to age and sex, and mortality per cent.*

Ages.	Males.			Females.			Total.		
	Admissions.	Died.	Mortality per cent.	Admissions.	Died.	Mortality per cent.	Admissions.	Died.	Mortality per cent.
Under 1 - -	68	25	36·8	59	18	30·5	127	43	33·9
1 to 2 - -	214	68	31·8	176	58	33·0	390	126	32·3
2 ,, 3 - -	270	68	25·2	292	79	27·1	562	147	26·2
3 ,, 4 - -	384	77	20·1	365	77	21·1	749	154	20·6
4 ,, 5 - -	414	87	21·0	410	71	17·3	824	158	19·2
Total under 5	1,350	325	24·1	1,302	303	23·3	2,652	628	23·7
5 to 10 - -	1,106	142	12·8	1,324	168	12·7	2,430	310	12·8
10 ,, 15 - -	379	16	4·2	423	25	5·9	802	41	5·1
15 ,, 20 - -	121	5	4·1	154	—		275	5	1·8
20 ,, 25 - -	60	2	3·3	98	—	—	158	2	1·3
25 ,, 30 - -	43	—		60			103	—	
30 ,, 35 - -	25	1		46	1		71	2	
35 ,, 40 - -	13	—		26	—		39	—	
40 ,, 45 - -	3	—	2·2	17	—	1·9	20	—	2·0
45 ,, 50 - -	1	—		6	—		7	—	
50 ,, 55 - -	—	—		3	1		3	1	
55 ,, 60 - -	2	1		1	—		3	1	
And upwards -	2	—		1	1		3	1	
Total - -	3,105	492	15·8	3,461	499	14·4	6,566	991	15·1

It will again be noticed that the mortality has fallen by one half.

TABLE VI.

Contrasts the total mortality of Diphtheria cases admitted into the Hospitals of the Metropolitan Asylums Board for the four years 1890 *to* 1893 *and for* 1898.

Ages.	Mortality per cent. Pre-Antitoxin Period (1890-93).	Mortality per cent. Anti-Toxin Period (1898).
Under 1	67·46	33·9
1 to 2	64·25	32·3
2 ,, 3	59·05	26·2
3 ,, 4	49·31	20·6
4 ,, 5	42·49	19·2
Total under 5	52·44	23·7
5 to 10	28·41	12·8
10 ,, 15	10·27	5·1
15 ,, 20	3·39	1·8
20 ,, 25	3·89	1·3
25 ,, 30	5·07	2·0
30 ,, 35	4·54	
35 ,, 40	11·11	
40 ,, 45		
45 ,, 50		
50 ,, 55		
55 ,, 60		
and upwards		
Total - -	30·39	15·1

It will be observed that for every age-group the percentage mortality in 1898 was less than one half of what it was in the pre-antitoxin period 1890 to 1893.

In a report issued by the Medical Superintendents of the Metropolitan Asylums Board for the year 1895, the following table (Table VII.) appears, which shows the great importance of the treatment being adopted at an early stage of the disease ; this we can readily see is in absolute accord with our scientifi knowledge of the cause and progress of the disease.

TABLE VII.

Showing percentage of mortality in relation to day of disease on which cases of Diphtheria came under treatment in the Hospitals of the Metropolitan Asylums Board in 1895.

Day of disease.	Mortality per cent.
First	11·7
Second	12·5
Third	22·0
Fourth	25·1
Fifth and over	27·1
Total	22·5

This table is not repeated in the 1898 report.

The benefits derivable from early treatment are clearly shown in this table. But far more striking evidence is obtained from the experience of the serum treatment of post-scarlatinal diphtheria cases, that is, cases of scarlet fever which develop diphtheria whilst in scarlet-fever wards. To such cases occurring in the Board's hospitals, the treatment can be applied immediately after the diagnosis of the disease.

The following table (Table VIII.) shows the percentage incidence of post-scarlatinal diphtheria, the case mortality, and the case mortality calculated on the scarlet fever cases for each year from 1892 in all the Board's hospitals.

TABLE VIII.

Giving number of cases of Post-Scarlatinal Diphtheria, case mortality, etc., in the years 1892 to 1898 in the Hospitals of the Metropolitan Asylums Board.

	1892.	1893.	1894.	1895.	1896.	1897.	1898.
Total number of completed scarlet fever cases	11,326	14,897	12,637	10,422	15,176	15,241	12,771
Number of cases of post-scarlatinal diphtheria	217	204	220	408	765	796	661
Percentage incidence	1·91	1·37	1·74	3·91	4·64	5·22	5·17
Number of deaths -	95	120	74*	58*	36	30	24
Case mortality -	43·8	58·8	33·6*	14·2*	5·1	3·7	3·6
Case mortality calculated on the scarlet fever cases	·84	·80	·6*	·55*	·23	·19	·18

It will be seen that the case mortality has been reduced from 43·8 and 58·8 per cent. in 1892 and 1893 to 3·7 and 3·6 per cent. in 1897 and 1898. These figures, perhaps, afford the most striking evidence of the efficacy of the treatment by antitoxic serum.

The following are summaries of tables which give the experience of Professor J. Sims Woodhead of the year 1896, during which time he was examining the throats of the diphtheria cases admitted into the Asylums Board's Hospitals, and show the influence of time in connection with the successful treatment of the disease.

Table IX. gives the percentage mortality at different ages of all cases in which the diphtheria bacilli were found during the year 1896.

* These figures are too low, since no return has been published for one of the hospitals in each of these years.

TABLE IX.

Percentage mortality at different ages of all cases that have been bacteriologically examined, and in which diphtheria bacilli were found. Day of disease, taken from Ambulance Nurse's Report, 1896.

SUMMARY.

Day of Disease.	1.		2.		3.		4.		5.		6.		7.		8 and upwards.		Total.		Mortality per cent.
Ages.	Cases.	Deaths.	Cases.	Deaths.	Cases.	Deaths.	Cases.	Deaths.	Cases.	Deaths.	Cases.	Deaths.	Cases.	Deaths.	Cases.	Deaths.	Cases.	Deaths.	
Under 1 - -	5	—	14	7	14	7	11	3	11	2	4	1	6	4	9	4	74	28	37·8
1 ,, 2 - -	3	2	40	17	65	27	46	22	34	13	20	11	8	5	25	14	241	111	46·0
2 ,, 3 - -	15	5	74	18	78	24	75	27	65	16	47	16	23	8	38	12	415	126	30·3
3 ,, 4 - -	49	3	103	14	119	24	107	33	81	19	78	29	36	7	62	17	635	146	22·9
4 ,, 5 - -	42	1	95	13	122	35	125	28	113	37	62	13	36	11	76	15	671	153	22·8
5 ,, 10 - -	222	8	283	19	359	56	367	64	264	54	181	39	130	34	222	41	2,028	315	15·5
10 ,, 15 - -	76	—	73	4	106	3	109	10	87	11	58	4	36	3	57	5	602	40	6·6
15 ,, 20 - -	16	—	16	—	35	—	23	2	29	3	13	—	6	—	9	1	147	6	4·1
20 and upwards	4	—	29	—	64	—	60	1	25	—	31	1	11	—	31	1	255	3	1·2
Total - -	432	19	727	92	962	176	923	190	709	155	494	114	292	72	529	110	5,068	928	—
Mortality per cent. - -	—	4·4	—	12 6	—	18·3	—	20·6	—	21·8	—	23·0	—	24·6	—	20·8	—	18·3	—

The general mortality was for each day as under :

TABLE IX. *a.*

Day of Disease.	1.	2.	3.	4.	5.	6.	7.	8 and upwards.	Total.
Total cases -	432	727	962	923	709	494	292	529	5,068
Total deaths -	19	92	176	190	155	114	72	110	928
Mortality per cent. - -	4·4	12·6	18·3	20·6	21 8	23·0	24·6	20·8	18·3

Table X. gives the percentage mortality at different ages of all cases in which *no* diphtheria bacilli were found.

TABLE X.

Percentage mortality at different ages of all cases that have been bacteriologically examined, and in which no diphtheria bacilli were found. Day of disease taken from Ambulance Nurse's Report, year 1896.

SUMMARY.

Day of Disease.	1.		2.		3.		4.		5.		6.		7.		8 and upwards.		No History.		?		Total.		Mortality per cent.
Ages.	Cases.	Deaths.	Cases.	Deaths.	Cases.	Deaths.	Cases.	Deaths.	Cases.	Deaths.	Cases.	Deaths.	Cases.	Deaths.	Cases.	Deaths.	Cases.	Deaths.	Cases.	Deaths.	Cases.	Deaths.	
Under 1	1	—	5	4	5	2	6	2	3	—	2	1	—	—	3	2	–	—	1	1	26	12	46·2
1 to 2	1	—	12	4	15	5	11	3	9	2	5	2	4	2	18	8	–	—	–	—	75	26	34·7
2 ,, 3	4	1	11	4	18	7	23	4	17	4	11	5	11	1	18	6	1	—	1	1	115	33	28·7
3 ,, 4	9	—	17	1	26	4	21	4	21	4	12	3	11	3	34	8	1	—	–	—	152	27	17·8
4 ,, 5	13	1	16	1	30	4	26	4	22	3	20	4	16	3	33	8	1	1	1	1	178	30	16·9
5 ,, 10	50	2	45	4	85	8	84	5	53	6	54	3	39	1	78	8	1	—	3	—	492	37	7·5
10 ,, 15	25	1	32	—	52	1	57	2	38	3	34	—	13	2	37	4	1	—	1	—	290	13	4·5
15 ,, 20	12	—	20	—	35	—	33	1	24	1	19	1	6	—	22	—	1	—	2	—	174	3	1·7
20 and upwards	11	—	36	1	40	1	48	—	44	—	21	1	25	1	35	2	1	—	1	—	262	6	2·3
Total	126	5	194	19	306	32	309	25	231	23	178	20	125	13	278	46	7	1	10	3	1,764	187	—
Mortality per cent.	—	4·00	—	9·8	—	10·5	—	8·1	—	10·0	—	11·2	—	10·4	—	16·5	–	14·3	–	30·0	—	10·6	—

The general mortality (Table X. *a*) was for each day as under :

TABLE X. *a*.

Day of Disease.	1.	2.	3.	4.	5.	6.	7.	8 and upwards.	Total.
Total cases -	126	194	306	309	231	178	125	278	1,764
Total deaths -	5	19	32	25	23	20	13	46	187
Mortality per cent. - -	4·00	9·8	10·5	8·1	10·0	11·2	10·4	16·5	10·6

Table XI. gives the percentage mortality at different ages of all cases in which diphtheria bacilli were found, and antitoxic serum was injected.

TABLE XI.

Percentage mortality at different ages of cases in which diphtheria bacilli were found, and in which antitoxic serum was injected. In the first line is given the day on which antitoxic serum was injected, reckoning this from the appearance of the initial symptoms as reported by the Ambulance Nurse, year 1896.

SUMMARY.

Day of Injection.	1.		2.		3.		4.		5.		6.		7.		8 and upwards.		Onset in Hospital.		?		Total.		Mortality per cent.
Ages.	Cases.	Deaths.	Cases.	Deaths.	Cases.	Deaths.	Cases.	Deaths.	Cases.	Deaths.	Cases.	Deaths.	Cases.	Deaths.	Cases.	Deaths.	Cases.	Deaths.	Cases.	Deaths.	Cases.	Deaths.	
Under 1 - -	4	—	6	2	10	5	6	2	11	4	4	1	4	2	7	2	3	1	–	—	55	19	34·5
1 to 2 - -	3	2	33	14	37	14	40	20	22	7	16	9	9	7	16	9	9	4	3	2	188	85	45·2
2 ,, 3 - -	7	2	54	12	54	16	54	24	49	12	29	11	17	8	28	9	11	1	2	1	305	92	30·2
3 ,, 4 - -	35	2	58	4	94	18	78	24	59	18	53	22	24	14	50	16	27	4	4	2	482	116	24·0
4 ,, 5 - -	26	—	59	10	79	20	90	25	79	32	48	10	28	16	56	12	23	4	4	—	492	124	25·2
5 ,, 10 - -	162	6	164	15	227	50	261	55	182	51	124	26	84	30	126	34	54	2	6	2	1,390	266	19·1
10 ,, 15 - -	47	1	28	—	52	2	50	11	44	8	27	3	20	6	26	5	8	1	1	1	303	34	11·2
15 ,, 20 - -	7	—	7	—	8	—	5	1	5	2	8	1	4	—	1	—	1	—	–	—	46	5	10·9
20 and upwards -	3	—	6	—	20	—	17	1	13	—	11	1	3	1	5	1	2	—	–	—	80	3	3·7
Total - -	294	13	415	57	581	125	601	163	464	132	320	84	193	84	315	88	138	17	20	8	3,341	744	—
Mortality per cent.	—	4·4	—	13·7	—	21·5	—	27·1	—	28·5	—	26·2	—	43·5	—	27·9	—	12·3	–	40·0	—	22·3	—

The general mortality (Table XI. *a*) was for each day as under:

TABLE XI. *a*.

Day of Infection.	1.	2.	3.	4.	5.	6.	7.	8 and upwards.	Total.
Total cases	294	415	581	601	464	320	193	315	3,341
Total deaths	13	57	125	163	132	84	84	88	744
Mortality per cent.	4·4	13·7	21·5	27·1	28·5	26·2	43·5	27·9	22·3

Table XII. gives the percentage mortality at different ages of all cases in which *no diphtheria bacilli* were found, but in which antitoxic serum was injected.

TABLE XII.

Percentage mortality at different ages of cases in which no diphtheria bacilli were found, but in which antitoxic serum was injected. In the top line is given the day on which the antitoxic serum was injected, reckoning this from the appearance of the initial symptoms as reported by the Ambulance Nurse, year 1896.

SUMMARY.

Day of Injection.	1.		2.		3.		4.		5.		6.		7.		8 and upwards.		Onset in Hospital.		Total.		Mortality per cent.
Ages.	Cases.	Deaths.	Cases	Deaths.	Cases.	Deaths.	Cases.	Deaths.	Cases.	Deaths.	Cases.	Deaths.	Cases.	Deaths.	Cases.	Deaths.	Cases.	Deaths.	Cases.	Deaths.	
Under 1	1	—	3	2	2	1	2	—	—	—	—	—	—	—	3	1	1	—	12	4	33·3
1 to 2	1	—	4	1	4	2	4	1	5	1	3	2	1	—	11	6	2	1	35	14	40·0
2 ,, 3	1	—	4	1	2	1	11	3	11	2	5	3	4	2	9	2	1	—	48	14	29·2
3 ,, 4	4	—	2	—	7	2	3	2	9	3	6	2	4	3	10	5	3	—	48	17	35·5
4 ,, 5	8	—	4	—	5	1	10	3	10	3	6	2	2	—	10	3	2	1	57	13	22·8
5 ,, 10	17	1	9	—	20	5	20	3	11	2	7	2	9	—	26	5	4	—	123	18	14·6
10 ,, 15	7	—	2	—	8	1	11	—	9	2	3	—	4	1	7	2	1	—	52	6	11·5
15 ,, 20	4	—	1	—	3	—	2	—	1	—	3	2	—	—	3	—	—	—	17	2	11·8
20 and upwards	5	—	2	—	—	—	3	—	5	—	3	1	4	—	3	1	—	—	25	2	8·0
Total	48	1	31	4	51	13	66	12	61	13	36	14	28	6	82	25	14	2	417	90	21·6
Mortality per cent.	—	2·08	—	12·9	—	25·5	—	18·2	—	21·3	—	38·9	—	21·4	—	30·5	—	14·3	—	21·6	—

The general mortality was for each day as under :

TABLE XII. *a*.

Day of Infection.	1.	2.	3.	4.	5.	6.	7.	8 and upwards.	Total.
Total cases -	48	31	51	66	61	36	28	82	417
Total deaths -	1	4	13	12	13	14	6	25	90
Mortality per cent. - -	2·08	12 9	25·5	18·2	21·3	38·9	21·4	30·5	21·6

The advantage gained over former methods of treatment by the use of antitoxin in cases of laryngeal diphtheria are also most marked, and are clearly shown in Table XIII.

TABLE XIII.

Cases of Laryngeal Diphtheria in the Hospitals of the Metropolitan Asylums Board, 1895 *to* 1898, *together with mortality.*

Year.	Cases.	Deaths.	Mortality per cent.
1894 - -	466	289	62·0
1895 - -	468	196	41·8
1896 - -	516	153	29·6
1897 - -	491	152	30·9
1898 - -	654	225	34·4

The general death-rate of diphtheria in 1894 was slightly lower than in any previous year, and in the last few weeks of the year antitoxin was tentatively employed in most of the hospitals of the Asylums Board.

Table XIV. gives the number of tracheotomy cases which occurred during the same period in the hospitals of the Board, the number of deaths, and the mortality per cent. each year from 1894 to 1898:

TABLE XIV.

Cases of Tracheotomy in the Hospitals of the Metropolitan Asylums Board, 1895 *to* 1898, *together with mortality.*

Year.	Cases.	Deaths.	Mortality per cent.
1894 - -	261	184	70·4
1895* - -	255	125	49·4
1896 - -	212	87	41·0
1897 - -	264	107	40·5
1898 - -	313	119	38·0

From a consideration of these tables it is manifest that the greatest success attended the treatment of those cases which were at once recognised, and immediately subjected to the injection of antitoxic serum.

We have now arrived at the stage where we may conveniently consider what, if any, practical points we have gleaned which may be of service to us in dealing with outbreaks of this disease.

We naturally ask, How is its continuity maintained in the intervals between epidemics? Is it a sufficient explanation to say that the disease is kept alive by direct infection from one to another by so-called unrecognised cases? or is it not more reasonable to suppose that the germ finds some favourable local habitat such as soil, and that at intervals its virulence becomes increased and a fresh outbreak occurs? But if this be so, our inquiry is thrown a step further back, for we then have to determine what is the cause of the periodic increase of virulence, or else, assuming there is no variation in virulence, what occasions an attack on human beings? All these questions involve problems of the greatest complexity, which will still further have to be worked out.

* First antitoxin year.

The chief cause of infection, so far as our evidence at present goes, is personal contact. Owing to the compulsory notification of disease in this kingdom, there is but little chance of a well-marked case of diphtheria remaining for any time as a source of danger to the community, but there is a risk of mild and unrecognised cases so remaining; such, for example, as when one member of a family has contracted diphtheria, and has infected the other members, these latter being to some extent immune, or has infected others before definite symptoms have arisen necessitating isolation; or, secondly, amongst school-children, when a child has the specific organism in his throat and infects others before definite symptoms have arisen in the child's own person; or, thirdly, when convalescent patients who have been treated in hospital, are clinically cured, but still retain diphtheria bacilli on their fauces, and are allowed to return to their families.

As regards the first class of case, it would perhaps seem too herculean a task to examine bacteriologically the throat of every member of an infected household, especially as a single negative culture is insufficient to guarantee an absence of bacilli, but the plan adopted in the city of Providence, which has already been quoted, namely to require a negative culture from the throat of every member of a family that contains members of a public elementary school, is undoubtedly an excellent one. It might be found possible to adopt a similar system in London among the families of children attending schools. Moreover, if facilities were generally afforded to the medical attendants of families of a higher class to have bacteriological examinations made free of charge at a proper institution as is done in some cities, a large number of individuals who were capable of spreading the disease, although apparently healthy, might be traced.

I am aware that this Institute has urged upon the Metropolitan Asylums Board the desirability in the public interest of dealing with these questions in London by the provision of a laboratory where such problems could be adequately dealt with, but hitherto without success. Such an institution would be of the greatest value, not alone from the various points of view I have suggested, but also as affording an opportunity of carrying on the very

valuable investigations which the Board have already caused to be made. Systematic and uniform work in such an extensive and unparalleled field as London affords would doubtless advance our knowledge as to the infectivity of the different forms of bacilli, about which there is at present some confusion, and might possibly suggest further means of checking personal infection. The Metropolitan Asylums Board has done much to deserve the approval of the people of London in the past by the splendid provision it has made for the gratuitous treatment of the infectious sick of the Metropolis; it would, I venture to say, deserve our gratitude still more if the unique opportunities it has for dealing with many of the unsolved problems in connection with infectious diseases were utilized, and investigations undertaken in the manner I have indicated.

Then there is the danger arising from convalescent patients whose throats still harbour the specific germ. Professor Sims Woodhead has shown how long a time the bacillus will remain about the fauces of hospital cases. The throats of the medical officers and nurses in diphtheria wards also often contain the bacilli. In fact, it is almost surprising that the bacilli disappear in some patients in the course of a few weeks, for the throat is a part of the body which it is practically impossible to thoroughly sterilize by antiseptic sprays or washes.

Now, if it were insisted that no patient should be discharged till the throat were free from the specific germ, it would involve great hardship to the patient, and would put even a greater strain on hospital accommodation than is the case at present. The best thing would seem to be to send each patient, as soon as he was well enough, from the ward tenanted by acute cases, into the country if possible, or at all events into a different department of the hospital, and there, by means of abundance of pure air, aided by local antiseptic treatment, to see if the bacilli would not disappear in a shorter time than occurs in a diphtheria ward.

H. Richardière and L. Tollemer have made an interesting series of experiments for the purpose of determining whether bacilli were present in the air of apartments devoted exclusively to the

treatment of diphtheria patients before and after disinfection had been practised. These observations were made in the Bretonneau pavilion of the Hôpital Trousseau. In the first series of experiments the wards had not been disinfected for several weeks. They contained about thirteen diphtheria cases. Similar experiments were also made in apartments which had been occupied by diphtheria patients, but had subsequently been disinfected. The result of their observations showed that virulent diphtheria bacilli were present in the dust floating in the air of the Pavilion Bretonneau, which had not been disinfected for a long time, but that they were absent after disinfection. These experiments, therefore, show the importance of frequent disinfection of wards devoted to contagious cases, and the necessity for the precautions of rigid isolation such as is carried out in these wards at the present time. They show also that it is necessary to employ daily some means of removing, without at the same time stirring up, the dust of such apartments.—*Gazette des Maladies Infantiles*, 1899, No. 10.

We have noticed the great incidence of the disease on young children, and the importance of school authorities adopting all proper precautions for the prevention of the spread of the disease through the agency of schools. I have reasons for believing that these are not so rigidly observed throughout the country as they should be, and it would seem desirable that the Education Department should take a more active part in directing school authorities in these matters than they have hitherto done. Questions of the most vital public health interest are continually arising in connection with the aggregation of children in schools, and it would appear a matter of urgent public necessity that for such questions the Education Department should have at its disposal the services of an experienced medical adviser. I know that this Institute have made representations on the subject to the Government, and these it is to be hoped will meet with a favourable response.

But the measure of all others which I desire most strongly to urge is the use of diphtheria antitoxin for prophylactic purposes. Behring has shown, by direct experiment on goats and

other animals, that a dose of 200 antitoxin units will suffice to protect an animal perfectly for at least one month, and that even after this period the disease, if acquired, runs a comparatively mild course. These conclusions agree perfectly with those obtained in Heubner's Clinique. The prophylactic use of the serum has been taken advantage of largely on the Continent and in America, but little attention has been directed to the subject in this country.

Herman M. Biggs in 1897 stated that "diphtheria antitoxin was used largely for the immunization of the inmates of public institutions—especially those for children—when diphtheria has appeared. This is the routine practice, and in every instance during the last two years and a half it has been possible to quickly stamp out diphtheria in institutions by this process of immunization."

The only possible objection to its use is liability to the inconveniences occasionally attendant on the injection of the serum arising from the occurrence of rashes and perhaps joint pains. These are due not to the antitoxin, but to the serum itself, normal serums exerting a similar action, and, according to Behring, the smaller the amount of serum injected, the less is the risk of these symptoms occurring. The prophylactic dose, of course, requires only a very small quantity of serum, and Behring suggests that this ought to be reduced still more by the use of the extra potent serums, so as to obviate all risk of the occurrence of such symptoms. As these extra potent serums are not so stable as those of the lower grade, he suggests that for this purpose they should be sent out in the dry form.

Thus, 10 c.c. of a serum containing 500 units per c.c. can be dried to form a solid residue of one gramme, which can afterwards be easily dissolved in 5 c.c. of sterile water. The prophylactic dose of this solution would only be $\frac{1}{5}$ c.c. Its use may also be suggested in hospitals in the case of those scarlet fever patients exposed to the risk of diphtheritic infection and who so frequently acquire it, especially in the case of all those sent to the convalescent hospitals.

It is hardly necessary to state that the protection, where neces-

sary (as in the case of nurses, attendants, etc.), can be kept up by repeating the injection every five or six weeks.

By the general adoption of this means, I am certain, the amount of diphtheria would be materially diminished, much suffering prevented, and we should be fast approaching the time when the disease would be altogether removed from our midst.

APPENDIX.

Copy of a Letter to Professor William R. Smith, President of the Royal Institute of Public Health, Relative to the Question of School-Attendance and Propagation of Croup-Diphtheria.

Budapest: Office of Municipal Statistics,
November 25, 1899.

My dear Sir,

You have asked my opinion as to the probability of the increase of diphtheria and croup being dependent upon school-attendance, and especially as to whether the marked increase of croup-diphtheria in London, which has attracted no small amount of attention, could be regarded as being consequent upon the increase of elementary schools. On account of the time occupied by my work, and also of my being absent from Budapest on two occasions, I am only now in a position to satisfy your request.

Before dealing with the subject itself, let me first answer the other questions you asked:

1. Compulsory school-attendance has existed in Hungary since 1868, and consists of, firstly, lower elementary schools for children from 6 to 12; and, secondly, of repetitory schools (twice a week) for children from 12 to 14 who receive no other instruction.

In Budapest during 1897-98, 57,054 children from 6 to 12 attended the lower elementary schools, and 425 children attended the repetitory schools.

2. If any infectious disease appears with excessive frequency at a school, the latter may be closed by the Chief Officer of Health. ("*Oberphysicus.*")

3. Regarding prophylactic measures to prevent the propagation of epidemic diseases, you will find the necessary information in my book "Statistik der infectiösen Erkrankungen in den Jahren 1881-1891 und Untersuchung des Einflusses der Witterung," on p. 33.

I shall therefore limit myself here to mentioning that the

prophylactic measures include: The obligatory notification and expulsion from school of the sick child and other children of the same household; isolation of the patient, or, if isolation is impossible, removal to the special hospital for epidemic diseases; finally, disinfection of the house and furniture. This system of preventative measures was proposed by me in 1880, and has been in force since January 1, 1881.

The obligatory notification includes the following diseases: Diphtheria and croup, measles, scarlet fever, small-pox, typhus, and cholera; moreover, since 1889 varicella, dysentery, whooping-cough, erysipelas, trachoma, and puerperal fever were added; finally, since 1896 the following have been included: epidemic cerebro-spinal meningitis and mumps.

In each case the physician in attendance is required to attach a red warning bill to the door of the dwelling.

Passing now to the principal questions, viz., What may be the causes of epidemics of diphtheria, and is school-attendance to be regarded as one of them? I do not feel competent to enter into the former more bacteriological question. As to the second, I submit to you the following facts:

I. In the first place, one might, as you pointed out in your letter, compare the death-rates from diphtheria and croup at different ages, and from this find out whether the school-age is more affected than previous or subsequent ages. Let us try this method for Budapest. Table I. shows the number of deaths caused by diphtheria and croup together—the distinction of these two diseases offering some difficulties—between the last two censuses, that is, January, 1881, and January, 1891.

The number of people living has been taken as an average of the two censuses. As regards division into single age groups, we know it for the living population, but as for the dead, the scheme of our vital statistics returns the single years of age only during the first quinquennium, and then proceeds by quinquennial periods, so that I can furnish the death-rate at each age for the first five years of life only.

TABLE I.

Deaths caused by Diphtheria and Croup in the City of Budapest in the Years 1881-1890.

Years.	0-1 Year.	1-2 Years.	2-3 Years.	3-4 Years.	4-5 Years.	5-10 Years.	10-15 Years.	15-20 Years.	20 Years and over.	Total.
1881 - - - -	39	89	78	70	42	88	8	—	2	416
1882 - - - -	34	80	91	58	56	67	4	1	5	396
1883 - - - -	22	59	40	41	28	48	6	1	1	246
1884 - - - -	26	50	53	46	30	44	3	—	1	253
1885 - - - -	22	52	54	51	34	40	1	—	—	254
1886 - - - -	47	122	116	102	60	99	10	1	5	562
1887 - - - -	58	121	100	84	55	93	5	—	6	522
1888 - - - -	32	117	84	76	47	81	4	2	4	447
1889 - - - -	48	140	132	112	70	124	10	1	2	639
1890 - - - -	70	163	192	148	105	207	20	4	4	913
Total deaths 1881-1890 -	398	993	940	788	527	891	71	10	30	4,648
Yearly average - -	39·8	99·3	94·0	78·8	52·7	89·1	7·1	1	3	464·8

If we compare the number of deaths at the different ages with the (estimated) population of the living at the same age, we arrive at the following results:

CROUP-DIPHTHERIA.

Age.	Population.	Deaths per annum.	Death-rate.
0-1 year -	10,731	39·8	3·71 per cent.
1-2 years -	8,299	99·3	11·97 ,,
2-3 ,, -	8,356	94·0	11·26 ,,
3-4 ,, -	8,014	78·8	9·83 ,,
4-5 ,, -	7,610	52·7	6·92 ,,
5-10 ,, -	34,274	89·1	2·60 ,,
10-15 ,, -	34,492	7·1	0·20 ,,
15-20 ,, -	43,723	1·0	0·02 ,,
20 and over -	277,856	3·0	0·01 ,,
Total -	433,355	464·8	1·07 ,,

The figures show that the death-rate is greatest at the ages 1 to 3, reaching at this point 11 to 12 per cent.; it afterwards falls rapidly, and stands in the fifth year of life at 7 per cent.;

in the following quinquennial period at 2·6 per cent., whilst after the age of 10 years it is nearly zero.

From these death-rates it seems quite impossible to deduce any influence to school-attendance, as the great majority of the deaths (about four-fifths) occurs *before* the school-age, which begins at the sixth year. But we ought to be very cautious in a matter where effects are produced by so many causes. The influence of school-attendance cannot be judged by the mortality of the children at school, as this influence is not only a direct, but also an indirect one, since these school-children are at an age when, although exposed to diphtheria, they may remain themselves healthy, but yet infect the younger children at home. Further, it is possible that the infections occurring during the school-age would be still fewer without school-attendance. The uselessness of basing our observations on death-rates appears most clearly if we apply them to the case of measles, which, as will be immediately proved, is certainly spread by school-attendance. If, however, we calculate the death-rates, as above in the case of diphtheria, we should not suspect this fact, as is shown by the following results relating also to the decennium 1881-1891:

MEASLES.

Age.	Population.	Deaths per annum.	Death-rate.
0-1 year -	10,731	31·1	2·90 per cent.
1-2 years -	8,299	41·1	4·95 ,,
2-3 ,, -	8,356	21·8	2·61 ,,
3-4 ,, -	8,014	12·3	1·53 ,
4-5 ,, -	7,610	9·1	1·19 ,,
5-10 ,, -	34,274	7·7	0·22 ,,
10-15 ,, -	34,492	0·6	0·02 ,,
15-20 ,, -	43,723	0·3	0·01 ,,
20 and over -	277,856	1·1	0·00 ,,
Total -	433,355	125·1	0·29 ,,

Thus also with measles the great majority of cases occurs amongst children not yet at school. Besides this, we ought to remember that the fatality of infectious diseases is different at the

different ages. Consequently, all investigations ought to be based on the morbidity instead of on the mortality. *The comparison of death-rates at different ages is thus quite unsatisfactory.*

II. To investigate the influence of school-attendance on diphtheria morbidity, I prefer another method, which consists in the comparison of the propagation of this disease with that of another, which is undoubtedly caused and distributed by school-attendance. I refer to measles, which shows this dependency in a most apparent way, as proved in my book on infectious diseases quoted above. Referring to this book, I have extracted shortly the following proofs deduced from no less than 70,591 notified cases.

TABLE II.*

Measles Morbidity at Budapest, 1882-1898 (*showing also the minima and the maxima*).

Years.	Jan.	Feb.	March.	April.	May.	June.	July.	Aug.	Sept.	Oct.	Nov.	Dec.	Total.
1882 - -	302	299	**577**	**563**	498	337	159	*42*	*28*	*32*	48	78	2,963
1883 - -	*51*	*59*	155	217	**382**	355	196	95	91	147	204	184	2,136
1884 - -	170	377	767	**1,204**	**1,090**	536	233	*23*	*9*	*14*	42	80	4,545
1885 - -	51	58	52	67	104	64	*27*	*12*	*27*	210	973	**1·648**	3,293
1886 - -	**1,413**	962	559	469	318	322	221	74	63	*46*	*46*	*43*	4,536
1887 - -	*34*	*29*	43	60	119	142	286	96	151	476	1,037	**1,257**	3,730
1888 - -	**418**	352	338	368	**450**	349	243	101	*39*	*45*	146	199	3,048
1889 - -	171	96	188	76	92	86	100	*42*	*34*	100	337	**413**	1,735
1890 - -	218	266	695	1,039	**1,248**	539	205	66	*30*	78	162	221	4,767
1891 - -	118	107	125	146	247	409	347	117	*65*	126	**458**	380	2,645
1892 - -	181	492	**876**	814	**875**	567	225	93	*73*	148	*69*	*71*	4,484
1893 - -	156	199	263	328	**843**	**937**	472	217	*111*	262	357	297	4,442
1894 - -	194	284	364	492	**751**	**760**	372	115	*66*	239	395	472	4,504
1895 - -	346	286	158	146	197	187	158	*78*	116	423	**1,012**	**1,049**	4,156
1896 - -	**680**	602	634	**654**	467	376	200	*56*	*58*	104	243	283	4,357
1897 - -	343	701	**957**	796	**974**	720	286	*74*	*43*	*75*	211	370	5,550
1898 - -	342	*213*	355	371	355	489	556	348	405	1,867	3·238	1,161	9,700
Total - -	5,188	5,382	7,106	7,810	**9,010**	7,175	4,286	*1,649*	*1,409*	4,392	**8,978**	**8,206**	70,591
Yearly average	305	310	418	458	**530**	422	252	*97*	*82*	258	**528**	**482**	4,152
Daily average†	9·84	11·21	13·48	15·31	**17·10**	14·07	8·13	*3·13*	*2·76*	8·33	**17·60**	15·57	11·37

* In this table, as in Table III., the minimum and maximum deaths of each year are marked by italics and by thick type respectively.
† The seventeen years 1882-1898 including four leap years, the length of February is calculated to $28\frac{4}{17}$ days.

A most efficient proof of the spread of measles through school-attendance is presented by the fact that in each year there are one or two heavy epidemical outbreaks, and one or two sudden declines in the disease. But it is noticed that the first outbreak *regularly occurs some months after the holidays.* The schools at Budapest open on September 1, and the epidemic usually reaches its first height in November and December. At the end of the latter month the Christmas holidays commence, but in the subsequent months, and especially in March, April, May, and June, the epidemic reaches a second maximum. These maxima, thus, always occur some months after the opening of the schools. Out of the 26 monthly maxima (figured in Table II.), 21 occur in the five months of November (3), December (4), March (3), April (3), and May (8), and never, during the 17 years under observation, in the months of July, August, September, October, or February.

Passing from the maximum to the minimum, we obtain a still more decisive proof of the influence of the holidays upon the decline of measles. The chief holidays begin in the second half of June, and last up to the end of August. The second shorter ones begin some days before Christmas, and last 10 or 12 days.* Following this up, we find that, in the 17 years under observation (1882-1898), during the months of March, April, May, and June the epidemics have affected from 7,000 to 9,000 persons; in the month of July the number falls to 4,300, in August to 1,650, reaching the minimum of 1,400 cases in September, the first month of school-attendance. In the second month of school-attendance we find 4,400 cases, and in the following months even 8,000 to 9,000, whilst in the two months after the Christmas holidays (January and February) we again find only 1,300 and 1,400 cases of the disease.

Out of the 34 minimal months 7, 12, and 5 occurred in August, September, and October respectively, while 2 were in November, 2 in December, and 1 in July, and during 17 years of observation not a single minimum occurred in March, April, May, or June—that is, at the end of the school year.

Amongst the twelve months, three (July, August and September)

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* The effects of the Easter holidays are considered later.

come under the influence of the holidays, the rest under that of school attendance.

If we now collect the frequency of the occurrence of maxima and minima under the headings of holiday and school months respectively, we find that the maximum appeared

in the 3 holiday months	0 times	=	monthly average	0,
,, 9 school ,,	26 ,,	=	,, ,,	2·7;

whilst the minimum appeared

in the 3 holiday months	20 times	=	monthly average	6·7,
,, 9 school ,,	14 ,,	=	,, ,,	1·5.

These are the results obtained by consideration of whole months. In order to allow for their different lengths, we will proceed to the daily averages of the number of cases :

(*a*) *Period of the long holidays* (2-2½ *months*).

July, first month of holidays	8·13	daily number of cases	average per diem, 4·67.
August, second month of holidays	3·13	,, ,, ,,	
September, first month of school attendance	2·76	,, ,, ,,	

(*b*) *First period of school-attendance.*

October	8·33	daily number of cases	average per diem, 13·83.
November	17·60	,, ,, ,,	
December	15·57	,, ,, ,,	

(*c*) *Period of the Christmas holidays* (10-13 *days*).

January	9·84	daily number of cases	average per diem, 9·84.

(*d*) *Second period of school-attendance.*

February	11·21	daily number of cases	average per diem, 14·25.
March	13·48	,, ,, ,,	
April	15·31	,, ,, ,,	
May	17·10	,, ,, ,,	
June*	14·07	,, ,, ,,	

If we compare the period of the long holidays (3 months) with the rest of the year, we find: for 3 months of holidays a daily average of 4·67 cases of measles, and for 9 months of school-attendance a daily average of 13·62 cases of measles.

Thus we see that school-attendance trebles the number of cases of measles.

* In the second half of June the schools already begin to close.

This is no doubt a satisfactory proof of the influence exercised by school-attendance on the propagation of measles. The proportion would be still greater if the results were not altered by the fact that, whenever a measles epidemic became serious, the schools were closed, so that we have always to take into account such intermediate irregular holidays.

We ought also to take into consideration the influence due to the Easter holidays; but as their commencement varies from the second half of March to the second half of April, the comparison of the monthly morbidity could lead to no result. I therefore prefer to compare the morbidity which occurred a fortnight before, aud one, two, or three fortnights after the holidays, as this may be obtained from the tables in my above-mentioned book, where the cases of sickness are recorded day by day. Unfortunately, this daily registration, based on notifications by single bills sent to the Health Office, could not be continued later than 1888, since which year their transmission has been stopped. Even during this period of 7 years 5 are exceptional, namely, where the maximum of measles did not take place, as usual, in the month of May, but in 1882 and 1884 occurred in April, in 1885 and 1887 in December, while in 1886 it was in January, so that this unusual behaviour of the epidemic will confuse our conclusions. Notwithstanding this, we find that the progress of measles on the oue hand, and of croup-diphtheria on the other, are sensibly different. Measles, preparing for the great outbreak of the following month, shows a small rise during the six weeks following the holidays, whilst croup-diphtheria rises in the first fortnight, falls in the second, and rises again in the third, showing itself to be barely influenced by school-attendance. The figures are as follows :

*Morbidity caused by Measles (supposing there to be an Incubation of 5 Days).**

Year.	Duration of Easter Holidays.	1 Fortnight before Holidays.	Holidays.	First Fortnight after Holidays.	Second Fortnight after Holidays.	Third Fortnight after Holidays.
1882 -	April 2-10 - -	280	153	230	237	222
1883 -	March 18-26 -	75	62	86	121	152
1884 -	April 6-14 - -	550	379	568	504	421
1885 -	March 29 to April 6	27	22	31	53	53
1886 -	April 18-26 - -	243	101	158	152	180
1887 -	April 7-12 - -	20	13	47	53	55
1888 -	March 25 to April 3	231	137	155	168	224
	Total - -	1,426	867	1,275	1,288	1,307
	Daily average -	14·54	12·21	13·00	13·13	13·33

*Morbidity caused by Croup-Diphtheria (supposing there to be an Incubation of 5 Days).**

Year.	Duration of Easter Holidays.	1 Fortnight before Holidays.	Holidays.	First Fortnight after Holidays.	Second Fortnight after Holidays.	Third Fortnight after Holidays.
1882 -	April 2-10 - -	44	26	33	33	34
1883 -	March 18-26 -	26	24	28	19	21
1884 -	April 6-14 - -	23	19	30	24	19
1885 -	March 29 to April 6	22	14	28	13	20
1886 -	April 18-26 - -	33	15	34	36	46
1887 -	April 7-12 - -	34	8	19	30	27
1888 -	March 25 to April 3	28	17	34	29	32
	Total -	210	123	206	184	199
	Daily average -	2·14	1·73	2·10	1·87	2·03

* That is, counting the influence of holidays in 1882 from April 7 to 15, etc.

If we represent the holiday cases of sickness by 100, we should find these to be during

	Cases of Measles.	Cases of Croup-Diphtheria.
the first fortnight before the holidays	119·1	123·8
the Easter holidays - - -	100	100
the first fortnight after the holidays -	106·5	121·4
the second fortnight after the holidays	107·6	108·1
the third fortnight after the holidays	109·1	117·5

The Easter holidays reduced the morbidity from both diseases, but their progress after the holidays is quite different, so that we are entitled to suppose that there must be different causes at work in the two cases.

Let us here repeat my remark that this propagation of measles (by school-infection) could by no means be discovered by the above-mentioned method of comparing the mortality or morbidity at the school-age with that of earlier years, probably for the reason that this propagation is caused less by direct infection of the scholars than by the indirect infecting of the younger members of the family through them.

III. We have thus got in measles a type, a standard of a disease, which is propagated especially by school-attendance. Let us now compare with this standard the behaviour of croup-diphtheria. If this disease is also propagated by school-attendance, we should expect that its incidence during the periods of school-attendance and of holidays would vary in a manner analogous to that of measles. If this analogy cannot be found, then it is proved that the propagation of this disease is not influenced—that is to say, not mainly influenced—by school-attendance. I enclose a diagram showing the course on the one hand of measles, and on the other of croup-diphtheria, for each month from July, 1881, to December, 1898. A single glance at this diagram will show that, while measles presents a most striking yearly repetition of epidemic outbreaks, the other disease does not follow these lines. But as the general aspect of the numerous rises and falls, where the curves are sometimes opposite and sometimes parallel to one another, gives no clear

impression, I have tried to reduce the tables to figures by counting the number of times in which the curves follow a parallel or a contrary course. In this calculation I regard the condition as stable when the change in the number of cases of disease in the adjacent months is less than 5 per cent. in either direction, or where the numbers differ by only one case. In this way we arrive at the following results :

The 204 months observed furnish 203 changes, out of which measles showed—

(*a*) 102 falls in the number of cases in the following month.
(*b*) 98 rises ,, ,, ,, ,, ,, ,, ,,
(*c*) 3 "stable" months.

Croup-diphtheria showed in the corresponding positions—

(*a*) 53 agreements with the falls in measles and 49 disagreements (out of which there were 15 cases of stability).
(*b*) 54 agreements with the rises of measles and 44 disagreements (out of which there were 6 cases of stability).
(*c*) 0 agreements and 3 disagreements (where measles was "stable").

Consequently, there were 107 agreements and 96 disagreements. Thus we see, in the first place, that croup and diphtheria do not follow the rises and falls of measles. In the second place, these figures demonstrate the cause of the coincidences and discrepancies of the two curves; for the total number of the changes in the curves being 203, if the agreements and disagreements between that for measles and that for croup-diphtheria are regulated by chance only, we ought to expect $101\frac{1}{2}$ coincidences and $101\frac{1}{2}$ discrepancies. As a matter of fact, there are 107 of the first class and 96 of the second.

We may thus conclude that *the coincidence of measles and croup-diphtheria is regulated in nine-tenths of the cases by chance.*

IV. After the conclusions drawn from this diagram, let us now turn to tables of notifications. The following table (III.) is arranged in the same manner for croup-diphtheria as was Table II. for measles :

TABLE III.

Croup-Diphtheria Morbidity at Budapest, 1882-1898 (*maxima shown in thick type, minima in italics*).

Years.	Jan.	Feb.	March.	April.	May.	June.	July.	Aug.	Sept.	Oct.	Nov.	Dec.	Total.
1882 - -	**108**	57	**108**	79	66	78	*49*	*50*	*48*	60	85	58	846
1883 - -	57	47	64	61	48	48	*29*	*26*	38	49	51	**67**	585
1884 - -	**67**	**69**	57	62	43	41	*30*	*31*	*31*	36	48	47	562
1885 - -	50	*28*	57	63	50	38	*29*	*31*	41	46	53	**74**	560
1886 - -	62	*43*	63	66	57	94	64	75	102	**132**	121	100	979
1887 - -	80	78	63	*49*	63	*41*	51	59	76	93	**96**	**101**	850
1888 - -	68	74	60	*55*	*56*	*52*	*50*	71	71	71	**86**	**90**	804
1889 - -	89	76	*71*	*68*	77	*70*	75	122	122	106	**195**	**187**	1,258
1890 - -	*84*	99	167	175	161	158	139	152	190	329	**371**	**343**	2,368
1891 - -	233	180	198	178	238	181	*155*	*160*	241	**394**	**364**	305	2,827
1892 - -	243	262	245	**310**	262	209	215	194	216	209	*159*	*159*	2,683
1893 - -	**197**	*127*	135	188	**208**	140	132	146	146	**192**	180	*121*	1,912
1894 - -	**178**	137	139	154	145	111	116	109	*88*	128	149	150	1,604
1895 - -	103	123	104	123	110	93	86	*74*	124	**147**	**144**	**142**	1,373
1896 - -	117	108	**142**	94	91	79	88	73	96	83	91	*66*	1,128
1897 - -	84	68	**103**	86	63	*57*	63	77	74	89	74	82	920
1898 - -	93	92	**127**	72	101	*52*	70	61	57	108	116	88	1,037
Total - -	1,913	1,668	1,903	1,883	1,839	*1,542*	*1,441*	*1,511*	1,761	**2,272**	**2,383**	**2,180**	22,296
Yearly average	112	98	112	110	108	*90*	*85*	*88*	104	**133**	**140**	**128**	1,312
Daily ,,	3·61	3·47	3·61	3·69	3·49	*3·02*	*2·73*	*2·87*	3·45	**4·31**	**4·67**	**4·14**	3·59

Comparing the "totals" of Tables II. and III., we observe *that neither the maxima nor the minima coincide.* The maxima of measles, caused by school-attendance, occur, as above mentioned, some months after the holidays in November, December, April and May, whilst those of croup-diphtheria appear in the cold months,* but are very far from reaching such an excess as in the case of measles.

Still less concordant are the minima; for measles these occur in August and September, for croup-diphtheria in June, July and August, in the case of the latter disease caused by the high temperature, in the former by the holidays.

When dealing with measles, we grouped the months according to the influence of the holidays and school-attendance, and found that the latter almost trebles the morbidity of the disease. Let us now make the same arrangement for croup-diphtheria, and see if there will be a corresponding result.

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* I found that croup and diphtheria do not appear most frequently in the very cold seasons, but rather when the temperature is near the freezing point if coinciding with great humidity of air. I beg to be allowed to quote from my book, mentioned above ("Statistik der infectiösen Kreukheiten und Untersuchung des Einflusses der Wittering), the following results on the *combined* effect of temperature and humidity, based on the notifications received at Budapest in the seven years 1881-88 (the figures show the number of notified cases in a pentade):

(*a*) Croup 1,468 Cases (pp. 64-71).

Humidity of Air.	*Temperature.*					
	Very Cold (below freezing point).	Cold (0-5° C.)	Temperature (5-14° C.)	Warm (14-18° C.)	Hot (above 18° C.)	Total.
Dry (below 60%) ...	—	3·75	2·96	2·35	2·41	2·57
Wet (60-80%)	3·47	2·90	2·85	2·39	1·70	2·59
Very wet (above 80%)	3·37	3·24	2·49	2·43	—	3·07
Total	3·40	3·12	2·78	2·38	2·12	2·76

(*b*) Diphtheria 4,246 Cases (pp. 72-76).

Humidity of Air.	*Temperature.*					
	Very Cold (below freezing point).	Cold (0-5° C.)	Temperature (5-14° C.)	Warm (19-18° C.)	Hot (above 18° C.	Total.
Dry (below 60%) ...	—	8·50	7·76	7·50	6·97	7·27
Wet (60-80%)	7·73	9·08	8·20	6·63	5·65	7·40
Very wet (above 80%)	8·07	9·26	9·14	8·29	—	8·76
Total	7·95	9·15	8·36	7·—	6·42	7·75

The following are the figures :

(*a*) *Period of the long holidays* (2-2½ *months*).

July -	- 2·73 daily cases of disease		average per diem, 3·02.
August -	- 2·87	,, ,, ,,	
September	- 3·45	,, ,, ,,	

(*b*) *First period of school-attendance.*

October -	- 4·31 daily cases of disease		average per diem, 4·38.
November	- 4·67	,, ,, ,,	
December	- 4·14	,, ,, ,,	

(*c*) *Period of the Christmas holidays* (10-13 *days*).

January -	- 3·61 daily cases of disease	average per diem, 3·61.

(*d*) *Second period of school-attendance*

February -	- 3·47 daily cases of disease		average per diem, 3·46.
March -	- 3·61	,, ,, ,,	
April -	- 3·69	,, ,, ,,	
May -	- 3·49	,, ,, ,,	
June -	- 3·02	,, ,, ,,	

Comparing the period of the long holidays with that for the rest of the year, we find a daily morbidity of 3·02 for the former, as against 3·78 for the latter period. Thus, the period of school-attendance shows a slight increase of morbidity, which *perhaps* may be caused partly by school-influence, but might be partially explained by the fact that the first period of school-attendance occurs in the cold months, when, in consequence of the low temperature and humidity, cases of diphtheria and croup are most frequent. In order to elucidate this point, it would be desirable to arrange for observations, such as those made in Budapest, to be carried out in a climate where the months of October, November and December fall in the warm season. But our own observations show that during the second period of school-attendance, which occurs in the warmer months, the cases of disease from diphtheria and croup are diminishing, while those from measles are rising. And, finally, if we remember that measles increases from a daily average of 4·67 to one of 13·62,

representing a rise from 100 to 292, whilst croup-diphtheria increases at the same time only from 3·02 to 3·78, representing a rise from 100 to 125, we have an effective proof that there are different causes at work in the propagation of the two diseases.

After all these facts and conclusions, I can only reply to your question, as to whether school-attendance is to be regarded as the chief, or only as a prominent, cause of the propagation of croup-diphtheria, in the negative sense. No doubt it is obvious that infectious diseases are propagated by all meetings of great masses, and in this sense it cannot be denied that schools contribute to the spread of such diseases. But as it is impossible to stop all human commerce for the sake of prevention, we must ask ourselves if one of these agglomerations forms, indeed, the chief cause of the propagation of a sickness. In the case of measles, for instance, the propagation by means of schools is a very important one; but in that of croup-diphtheria, although it is quite possible that attendance at schools does contribute to a certain degree in spreading the disease, yet this contribution seems extremely weak, incomparably more so than in the case of measles. Thus, I agree fully with the conclusions of Dr. Newsholme ("Epidemic Diphtheria," London, 1898, p. 138), who, looking at the subject from quite a different point of view, and following quite a different method, arrived at the same result, namely: "that school-infection is only a minor cause of the spread of this disease." Thus, returning to the first question, viz., as to whether the erection of new schools in London may be regarded as the principal cause of the increase of croup-diphtheria, I can only say, after my experiences at Budapest, that this causality is not at all proved, and that the coincidence of the two phenomena is almost entirely a matter of chance.

I am, my dear Sir,

Yours very faithfully,

JOSEPH DE KÖRÖSY,

Director of Municipal Statistics.

Honorary Member of the London Royal Statistical Society.

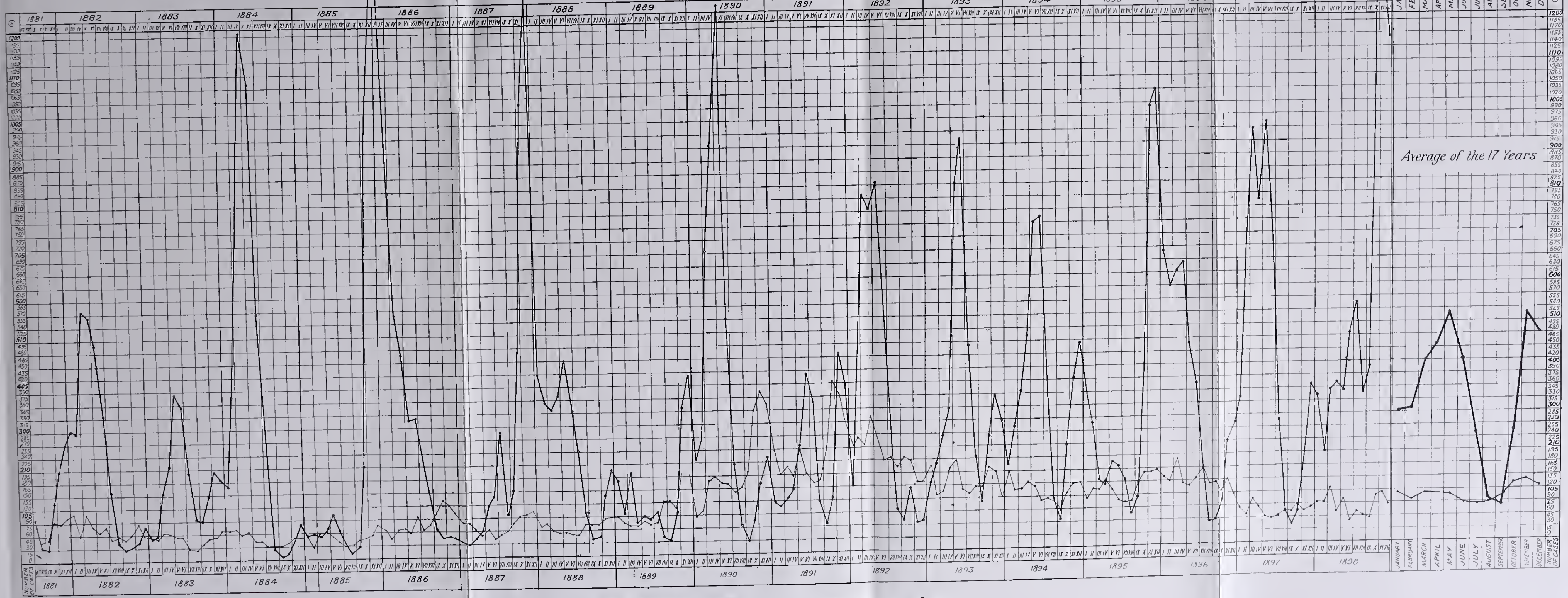
PROFESSOR WILLIAM R. SMITH, M.D., F.R.S. EDIN.,

President of The Royal Institute of Public Health.

MONTHLY MORBIDITY OF MEASLES AND CROUP-DIPHTHERIA AT BUDAPEST

1882 July 1 – 1898 December 31

by Dr. Josef de Körösy



THE LARGER CURVE IS THAT OF THE MEASLES MORTALITY